RESPIRATION AND VENTILATION OF INFANTS DURING ENDOTRACHEAL ANAESTHESIA

H. J. TEIJEN

Respiration and ventilation of infants during endotracheal anaesthesia

PROMOTOR: PROF. DR. J. F. CRUL

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To Anneke
and our boys

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$A\text{-}a\,P_{O_2}$: difference in partial oxygen pressure between alveolar air and arterial blood
BE : base excess
C : compliance of lungs, chest wall or respiratory system
Ca_{O_2} : ml oxygen in 100 ml arterial blood
$C\bar{v}_{O_2}$: ml oxygen in 100 ml true mixed venous blood
D : difference between values
Δ : change of a value (parameter)
η : viscosity constant
FA_{CO_2} : fractional concentration of carbon dioxide in alveolar air (%)
FI_{O_2} : fractional concentration of oxygen in inhaled gas (%)
FRC : functional residual capacity
IPNPV : intermittent positive-negative pressure ventilation
IPPV : intermittent positive pressure ventilation
LAP : left atrial pressure
P_{atr} : right atrial pressure
$\bar{P}_{atr}$: mean right atrial pressure
Pa_{CO_2} : partial carbon dioxide pressure in arterial blood
PA_{CO_2} : partial carbon dioxide pressure in alveolar air
PAP : pulmonary artery pressure
P_{oes} : oesophageal pressure
$\bar{P}_{oes}$: mean oesophageal pressure
P_{trach} : intratracheal pressure
$\bar{P}_{trach}$: mean intratracheal pressure
$P\bar{v}_{CO_2}$: partial carbon dioxide pressure in true mixed venous blood
$\dot{Q}$: volume flow of blood per unit of time
$\dot{Q}s$: volume of pulmonary shunt blood per unit of time
$\dot{Q}t$: total cardiac output
R : resistance
Sa_{O_2} : % oxygen saturation of Hb in arterial blood
$S\bar{v}_{O_2}$: % oxygen saturation of Hb in true mixed venous blood
SIV : Sheffield Infant Ventilator
SR : spontaneous respiration
TPP : transpulmonary pressure
$\overline{TPP}$: mean transpulmonary pressure
$\dot{V}A$: alveolar ventilation per minute
$\dot{V}_{CO_2}$: carbon dioxide production per minute
$\dot{V}E$: volume of exhaled gas per minute
$\dot{V}_{O_2}$: oxygen consumption per minute
VT : tidal volume

Introduction and problem definition

Endotracheal anaesthesia is a necessity in the surgical treatment of a number of conditions in infants. The dimensions of the respiratory tract in these patients are small, and insertion of an endotracheal tube causes an increase of the resistance to be overcome during respiration.

Rees (1950) pointed out that the respiratory mechanism in neonates is still poorly developed. The tracheal diameter is 3.6-5.7 mm, versus an adult value of 15-20 mm. There is virtually no costal breathing, and the ribs are in horizontal position. Respiration is chiefly diaphragmatic. This is why Rees attaches great importance to controlled ventilation during anaesthesia of infants, in order to minimize the energy which the patient must spend on ventilation. The use of muscle relaxants is unnecessary in these cases.

Stofregen (1960) likewise believes that the intubated infant should be aided by controlled ventilation during anaesthesia. However, since the elastic forces of the thorax are insufficient to ensure adequate passive expiration, the mean intrathoracic pressure can be so markedly increased as a result that the return of venous blood to the heart is impaired. This is why a subatmospheric pressure of 10 cm H_2O should be applied during the expiratory phase. According to Hennes and Waldeck (1963), expiration is so impaired by the resistance of the endotracheal tube that an increased functional residual capacity results. These authors maintain that the resistance in the pulmonary circulation is increased as well.

Pressure-flow diagrams of narrow endotracheal tubes of the kind used in infants, all show a degree of non-linearity (Glauser et al. 1961; Hutschenreuter 1962). This means that turbulence of the gas flow occurs in these tubes, as a result of which the respiratory resistance is increased. According to Keuskamp (1963), expiration in small infants is feeble, and they tire easily. This is why he agrees with Stofregen and Hutschenreuter that the expiratory resistance should be minimized, especially if controlled ventilation is employed. The use of a subatmospheric pressure in the expiratory phase is decidedly indicated in these cases, he maintains.

Reynolds and Etsten (1966), too, found an unmistakable influence of the endotracheal tube on respiratory work as determined during controlled ventilation.

The abovementioned views are counterbalanced by other opinions. Ayre, for example, argues as early as 1937 that, upon application of his T-piece system for endotracheal anaesthesia in hare-lip and cleft palate operations, 'there is no obstruction to free respiration; consequently no extra work is thrown upon the lungs and heart of a small baby'. Lunn (1968a) found a diminished respiratory minute volume in intubated, spontaneously breathing infants during a very light oxygen/nitrous

oxide/halothane anaesthesia. During surgical stimulation, however, hyperventilation was found to occur. Wawersik (1967) established an unmistakable influence of the resistance of the endotracheal tube on respiratory work in spontaneously breathing infants, but he considered them quite capable of coping with the extra work.

Thus we find controversial views on the importance of resistance in the respiratory tract due to the use of endotracheal tubes in infants, and on the importance of spontaneous respiration and controlled ventilation in this respect.

In our clinical work as anaesthetist to a neurosurgical team, we are being frequently confronted with the problems of longterm anaesthesia in infants. This is why it seemed of importance to us to acquire, by personal investigation, an opinion on the following questions:

a. is ventilation adequate during long-term endotracheal anaesthesia in infants, or is it not?
b. if not, does the resistance of the narrow endotracheal tube play an important role in this context?
c. what is the effect of intermittent positive pressure ventilation (IPPV) on the gas exchange and on the circulation?
d. is it of importance to resort to negative pressure during the expiratory phase?

If we are to answer these questions, we must be sure that the surgical intervention per sé exerts no direct influence on respiration. This eliminates patients to be treated by intra-abdominal or intrathoracic surgery from our study.

We studied infants – and sometimes slightly older children – who were treated for progressive hydrocephalus by a ventriculo-atrial shunt operation with the Spitz-Holter system. The thorax and abdominal cavity remain closed in this procedure. Through a cervical incision, a drain is passed into the right atrium via the right internal jugular vein. The proximal end of the drain is then guided beneath the skin towards the site at which the valve system is attached to the skull.

The sacrifice of an internal jugular vein proves not to influence the drainage of blood from the craniocervical region. If necessary, in fact, it is even possible to repeat the operation via the left internal jugular vein, without obstructing the efferent flow.

A Data from the literature on respiration in infants

1 ACID BASE STATE

Albert and Winters (1966) determined the blood gas values in capillary blood obtained 2-3 hours after the last feeding from 139 infants ranging in age from 2 to 24 months They found a Pa_{CO_2} of 33 8 ± 3 7 mm Hg, a base excess of −3 2 ± 1.7 meq/l and a pH act of 7 398 ± 0 027 With the exception of the pH, these values are low in comparison with those in adults As a possible explanation of this fact, these authors assumed that a discrepancy exists between the endogenous metabolic hydrogen ion production and the ability of the kidneys to excrete these ions The primary result of this would be reduction of the metabolic component of the acid-base balance, accompanied by a secondary reduction of the respiratory component with, as result, a normal blood pH The large production of H^+ ions might be related to the fact that, compared with adults, infants show a very high protein consumption on the basis of body weight 2-4 g/kg/day (Nelson 1966) Cook et al (1957) likewise found Pa_{CO_2} values between 25 and 40 mm Hg

Using an infra-red CO_2 meter, Blomer and Hahn (1963) determined a mean CO_2 concentration of 4 47% in the expiratory air in neonates within 7 days of birth In infants aged about 3 months, the values ranged from 3 09 to 4 93%, this corresponds with a Pa_{CO_2} of 22-36 mm Hg according to the equation

$$Pa_{CO_2} = FA_{CO_2} \times (760\text{-}47 \text{ mm Hg})$$

Accepting the CO_2 pressure as a yardstick of the sufficiency of ventilation, it can therefore be maintained that normal infants have a low Pa_{CO_2} in comparison with adults and therefore a relatively larger alveolar ventilation

2 VALUES FROM PULMONARY MECHANICS

During spontaneous respiration, active enlargement of the thoracic volume due to activity of the diaphragm, intercostal muscles and sometimes auxiliary respiratory muscles, creates a transpulmonary pressure which causes the lungs to expand and allows a certain gas volume to flow into them

The transpulmonary pressure is the difference between the intrapleural pressure and the pressure at the proximal end of the airway (Comroe et al 1955) The height of transpulmonary pressure is one of the factors determining the degree of lung stretch An inspiratory movement must overcome a the elastic resistance of the lungs, b the non-elastic, viscous resistance of the tissues, c the laminar and turbulent resistance of the gas flow, and d the extrathoracic resistance due to displacement of abdominal contents

The elastic and viscous resistance of the lungs determine the lung compliance. Strictly speaking, the compliance is a function of the intrinsic elastic characteristics of the lung tissue. In actual practice, however, the concept is understood in a wider sense, in which the degree of compliance can be determined by factors other than these intrinsic elastic characteristics alone (Davidson et al. 1970). Apart from the lungs, a compliance is also assigned to the thoracic wall and the combination of thoracic wall and thoracic contents. The relationship between these is given in the equation:

$$\frac{1}{\text{C, total respiratory system}} = \frac{1}{\text{C, lungs}} + \frac{1}{\text{C, thoracic wall}}.$$

Von Neergaard and Wirz (1927) sharply differentiated between static and dynamic compliance because they distinguished static from dynamic pleural pressure. If the compliance

$$C = \frac{\Delta V}{\Delta P},$$

then static compliance is the value found in the absence of gas movement in the air passages. Dynamic compliance is measured in the presence of a gas flow, in which case it is determined in part by the viscous and turbulent air flow resistance. The abovementioned investigators distinguished dynamic from static compliance as follows. They simultaneously recorded a pneumotachogram and a pleural pressure curve. The pleural pressures which correspond with the phase-change points of the pneumotachogram, indicate the static pressure corresponding with the lung volume in the inspiratory or expiratory state. Using this method, they were also the first to demonstrate that flow resistance during expiration exceeds that during inspiration. They ascribed this phenomenon to compression of the smallest bronchioles during expiration.

The lung compliance of infants is very small as compared with that of adults, for whom Comroe et al. (1955) reported a value of 200 ml/cm H_2O. Different authors have reported different values for infants.

In 18 infants with an average body weight of 3 kg, Cook et al. (1957) found a dynamic lung compliance of 5.2 ml/cm H_2O. Krieger (1963) determined a static lung compliance of 7.9 ml/cm H_2O in a group of 24 infants with a body weight of 2.7-11.7 kg. In view of the type of compliance measured it is understandable that the values determined by Cook et al. were lower than Krieger's.

Unlike the lung compliance, that of the thoracic wall is very large. Several investigators have determined it during endotracheal anaesthesia in infants ventilated with or without the aid of a muscle relaxant. Reynolds and Etsten (1966) found a dynamic compliance of 22.3 ml/cm H_2O; they used a pneumotachograph and determined the transpulmonary pressure from the difference between tracheal

and oesophageal pressure Lunn (1968b) found values between 17 2 and 31 2 ml/cm H_2O for the static compliance of the thoracic wall

The large compliance permits of very easy expansion of the thoracic wall during controlled ventilation The total compliance of the lung-thorax system is chiefly dependent on the value of the lung compliance The values found for the static lung-thorax compliance in the literature are 5 4 ml/cm H_2O (Nightingale and Richards 1965), and 2 77 ml/cm H_2O (Lunn 1968b) The dynamic compliance is 2 8 ml/cm H_2O according to Reynolds and Etsten (1966)

The respiratory resistance during spontaneous respiration was likewise determined by Cook et al in their abovementioned study The infants examined were in a quiet condition The mean value was 29 ± 0 4 cm H_2O/l/sec Krieger (1963) found an average inspiratory resistance of 22 cm H_2O/l/sec versus an expiratory resistance of 37 cm H_2O/l/sec For the combined resistance of inspiration and expiration she found the same value as Cook et al As in adults, therefore, the respiratory resistance in infants is greater during expiration than during inspiration The respiratory rates found in the abovementioned studies were 38 and 35 cycles/min, respectively Cook et al found a tidal volume which averaged 16 ml

Changes in intrapleural pressure occur during respiration or controlled ventilation Similar changes occur in the oesophagus The variations in oesophageal pressure in spontaneously breathing infants amount to 5 cm H_2O according to Cook et al (1957) and McIlroy et al (1955), whereas Krieger (1963) found 7 4 cm H_2O

3 RESPIRATORY WORK

The compliance of the adult lung is about 23 times as large as that of the infantile lung, but the resistance in the airway in infants is 10-15 times as large as that in adults These facts raise the question of the respiratory work in infants versus that in adults

The magnitude 'respiratory work/min' can be expressed in g cm/min The work involved in an inspiratory movement is the sum of the work required to overcome the viscous resistance of the lung, the laminar and turbulent resistance of the gas flow, and the elastic resistance of lungs and thorax The work involved in expiration is passive, it is provided by the potential energy contained in the expanded lungs and thoracic wall, and that in the abdominal contents displaced by the diaphragm However, the potential energy in thorax and abdominal contents can contribute but little due to the large compliance of these parts This energy is applied in order to overcome the viscous resistance of the lung and the resistance met by the gas flow As we explained, this factor is larger during expiration than during inspiration (fig 1)

Otis, Fenn and Rahn (1950) demonstrated that respiratory work is partly dependent on respiratory rate They placed adult test subjects in a Drinker respirator, and

determined the total, elastic, viscous and turbulent work; and they presented an equation indicating the relationship between these magnitudes. In a study of the respiratory work in infants, Cook et al. (1957) made use of this equation, but in a form so simplified that the magnitudes viscous work and turbulent work were represented by a single factor. This gave the following equation:

$$\text{Work/min} = \frac{1}{2C} f\,(V_T)^2 + \frac{Kr}{4}\,\pi^2 f^2\,(V_T)^2\ \text{g cm/min},$$

in which C is the compliance of the respiratory system, Kr is the resistance in cm H_2O/ml/min, f is the respiratory rate, and V_T is the tidal volume.

This equation clearly demonstrates the dependency on respiratory rate. In infants, the minimum work is provided at a respiratory rate of 37 cycles/min (fig. 2). According to McIlroy (Cook et al. 1957), respiratory work in infants can also be calculated on the basis of the equation Work/min = 0.6 $P\dot{V}_E$.

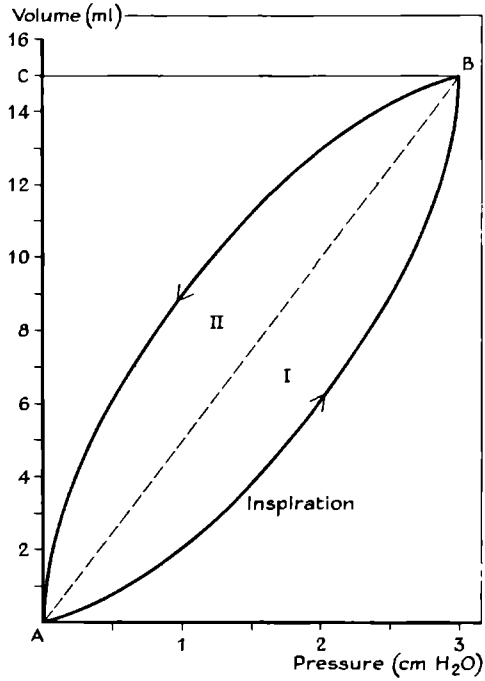

Fig 1 Diagrammatic average normal pressure-volume respiratory loop Elastic work is represented by area of triangle ABC Inspiratory and expiratory flow-resistive work are represented by areas I and II, respectively Assuming that expiration is passive, total pulmonary work is represented by the sum of the elastic work (triangle ABC) plus the inspiratory flow-resistive work (area I) The flow-resistive work represented by area II is covered by the energy stored in the elastic lung during inspiration

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In an absolute sense, there are great differences in the parameters of pulmonary mechanics between infants and adults. Cook et al. (1957) gave the following figures.

	Infant	*Adult*
weight (kg)	3	70
respiratory rate/min	38	15
tidal volume (ml)	19	
compliance (ml/cm H_2O)	5·2	170
resistance (cm H_2O/l/sec)	29	2
respiratory work (g cm/min)	1380	15·00*

* This value was calculated with the aid of the simplified equation of Otis et al (1950) The figure thus obtained is low because it does not account for turbulent flow resistance

In relative terms there are also similarities in lung function values between infants and adults. The specific compliance $\frac{C}{FRC}$ in infants and adults, respectively, is 0.065 and 0.068 ml/cm H_2O per ml functional residual capacity. The FRC is related to size. For infants, the FRC can be calculated by means of the formula $0.598 \times ht^3 \times 10^{-3\cdot5}$.

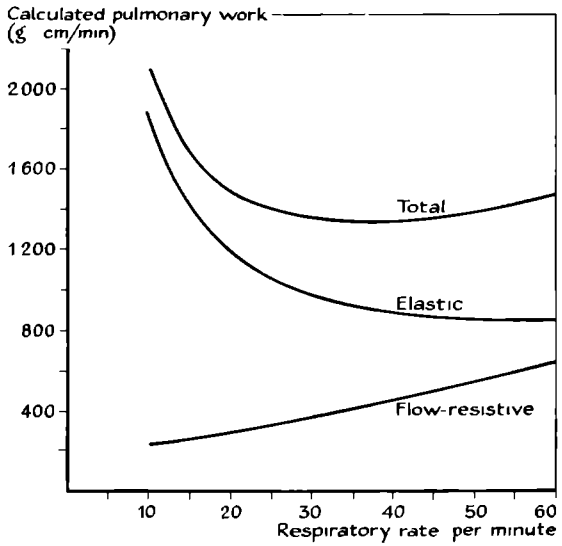

Fig 2 Calculated pulmonary work versus respiratory rate The theoretical pulmonary work at constant alveolar ventilation was calculated for various respiratory rates from the simplified formula of Otis, Fenn and Rahn The value used for respiratory dead space was 5·5 ml, alveolar ventilation 385 ml, compliance 5·2 ml/cm H_2O, and for resistance 29 cm H_2O/l/sec The theoretical minimum work of respiration occurs at a rate of 37 per minute

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Krieger (1963) compared adult with infantile respiration by relating the parameters tidal volume, minute volume and respiratory work to the body surface in square metres. She determined work to be 19,467 g cm/min/m^2 in infants, and found a value of 17,650-23,500 g cm/min/m^2 in adults. The values for minute volume/m^2 likewise showed agreement: 4203 ml/m^2 in infants and 4400 ml/m^2 in adults.

Thus, in spite of small lung compliance and a high airway resistance, the infant minimizes respiratory work by ventilating with a small tidal volume and at a high respiratory rate. These two parameters are reciprocally so adjusted as to ensure a minimum of respiratory work (McIlroy and Tomlinson 1955; Cook et al. 1957; Krieger 1963). The fraction of total work which is used to overcome elastic resistance is the same as that in adults (McIlroy and Tomlinson 1955), and amounts to about 70%.

In summary, we present some values from the literature on the respiratory physiology of infants in table I.

Table I Data on the respiratory physiology of infants

	Cook et al (1957)	Cook et al (1955)	McIlroy & Tomlinson (1955)	Krieger (1963)
Weight (kg)	3.0	2.5		
Respiratory rate/min	38	34		
V_T (ml)	16	15		
$\dot{V}_E$ (ml)		498	578	
$\dot{V}_A$ (ml)		355		
Amplitude P_{oes} (cm H_2O)	5.0	5.0	5.0	
C,l (ml/cm H_2O)	5.2			
R (cm H_2O/l/sec)	29			29
Work (g cm/min)	1380	1450	2600	
Work (g cm/m^2/min)				19,467
% Elastic work	70			68
$\dot{V}_{O2}$		17		
$\dot{V}_{CO2}$		12.3		

According to Harrison (1964) and Wawersik (1967), the pneumotachogram in young infants shows a sinus wave. The inspiratory peak flow is 3.14 × $\dot{V}_E$, and the ratio between inspiratory time and expiratory time is 1:1.

B Data from the literature on the influence of endotracheal intubation and anaesthesia on respiration in infants

1 INFLUENCE OF INTUBATION ANAESTHESIA AND CONTROLLED VENTILATION ON LUNG COMPLIANCE RESISTANCE IN THE RESPIRATORY TRACT RESPIRATORY WORK AND LUNG VOLUME

During endotracheal anaesthesia with controlled ventilation, the lung compliance is found to be diminished In a study of infants relaxed with the aid of d-tubocurarine (mean weight 3 4 kg), Lunn (1968b) found a static lung compliance of 3 13 ± 1 0 ml/cm H_2O

In a previously quoted study by Reynolds and Etsten (1966), the pulmonary mechanics of 15 infants were studied The test subjects weighed 3 8 kg on average and were intubated with a 14 French or 16 French endotracheal tube* They had been anaesthetized with a mixture of oxygen, nitrous oxide and halothane and were submitted to mechanical Intermittent Positive Pressure Ventilation (IPPV) The parameters measured were

a gas flow, with the aid of a pneumotachograph, b pressure at the junction between endotracheal tube and pneumotachograph, c oesophageal pressure Using the method of Von Neergaard and Wirz (1927), modified to measure oesophageal pressure instead of intrapleural pressure, they found a static lung compliance of 3 1 ml/cm H_2O and a dynamic lung compliance of 3 3 ml/cm H_2O The difference between these values was not statistically significant The resistance in the air passages, including the viscous tissue resistance, was found to be greatly increased 63 9 ± 3 7 cm H_2O/l/sec The calculated work was likewise high 6499 g cm/min, this was ascribed to the diminished lung compliance in combination with the greatly increased resistance in the air passages The latter was ascribed chiefly to the effect of the added resistance of the narrow endotracheal tube Turbulent flows easily occur in such narrow tubes, and this contributes to a further increase in resistance (Gaensler et al 1952) According to Reynolds and Etsten, therefore, the ventilation pressure used in IPPV is not a reliable indication of the efficacy of lung inflation in clinical anaesthesia In other words the ventilation pressure per se is not a good parameter for the transpulmonary pressure on which lung expansion depends (Maloney and Whittenberger 1957)

Reynolds and Etsten ascribed the low compliance values found to a decrease in pulmonary dimensions during anaesthesia, with or without alveolar collapse It was established by Forrest (1970) that hyperventilation can cause reduction of the total alveolar volume and total alveolar surface area, the total alveolar duct volume

* In our study we made use of latex endotracheal armoured plain tubes (Rusch product) size 14 French or 16 French These tubes have an internal diameter of 2 5 and 3 0 mm, respectively, and a length of 15 3 and 15 8 cm, respectively

remains unchanged. These findings are suggestive of diminution of the lung compliance. Forrest obtained his results by ventilating living anaesthetized guinea-pigs, which were then frozen to a temperature of $-170°$ C. He then employed a morphometric method to calculate the alveolar volume and alveolar duct volume of resected lung specimens. McClenahan (1966) believed that hyperventilation gives rise to an increased consumption or a change of alveolar surfactant; this would explain the diminution of compliance.

A study by Patterson and Sullivan (1968) disclosed that, during controlled ventilation, the lung compliance is influenced also by the PA_{CO_2} and the Pa_{CO_2}. In patients submitted to total cardiopulmonary bypass they demonstrated that a low PA_{CO_2} (less than 1%) results in an increase in respiratory resistance and a decrease in compliance. These changes are more marked at a normal than at a low Pa_{CO_2}. They determined the dynamic compliance on the basis of: a. the airway pressure at the mouth; b. the oesophageal pressure; c. the tidal volume; d. the gas flow rate.

Introduction of an increased resistance in the air passages can change the type of respiration so that mean lung volume and functional residual capacity increase.

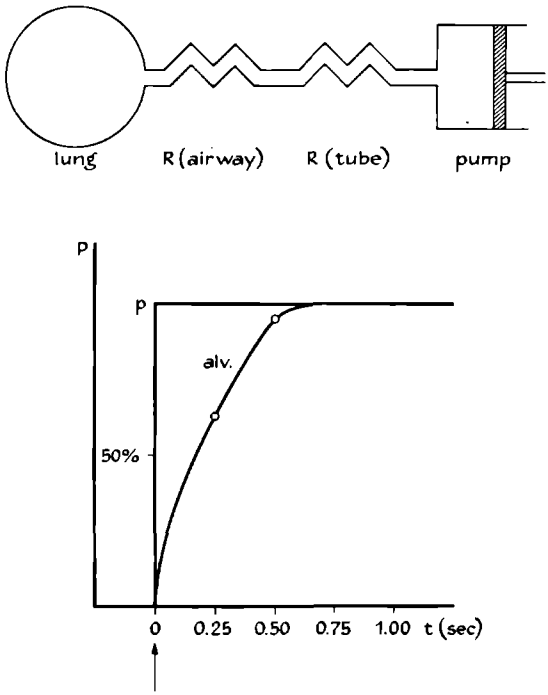

Fig. 3: Schematic representation of a pump-tube-airway system. The internal diameter of the tube is 2.8 mm, its length being 15 cm. A value of 5 ml/cm H_2O is assumed for the static lung compliance. It is assumed that inflation pressure P(p) is attained in 0 sec, and that a laminar air flow is induced. After 0.5 sec, P(alv) = 0.95 P(p) applies to intra-alveolar pressure.

Whittenberger (1951) demonstrated this in a test subject breathing into a spirometer through a narrow tube Gaensler et al (1952) recorded the same phenomenon with the aid of a Carlens double lumen catheter The phenomenon also becomes manifest when an anaesthetized test subject is abruptly exposed to an expiratory resistance (Campbell and Howell 1962) The increased potential energy in the more expanded lungs can serve to overcome the expiratory resistance

The findings reported by Reynolds and Etsten (1966) raise the question of the interval between a change in ventilation pressure and the resulting change in alveolar pressure Our basic assumption is that the pump pressure is attained in 0 sec, the pump pressure (ventilation pressure) will be followed by the alveolar pressure with some slight delay (fig 3)

The rate at which the alveolar pressure attains the plateau is dependent on

$$C_{lung\ stat} \times (R_{airway} + R_{tube})$$

On the basis of the data supplied by Cook et al (1957) it can be stated that

$$C_{lung\ stat} = 5\ cm^3/cm\ H_2O$$
$$= 0\,005\ cm^4\ sec^2\ g^{-1} \quad \text{(40 times smaller than in an adult)}$$

$$R_{airway} = 30\ cm\ H_2O/l/sec$$
$$= 30\ g\ cm^{-4}\ sec^{-1} \quad \text{(15 times larger than in an adult)}$$

$$R_{tube} = \frac{8\,\eta\,l}{\pi r^4}$$
$$= \frac{8 \times 2 \times 10^{-1} \times 15}{\pi \times 4 \times 10^{-4}} \quad (\eta \text{ for air } 2 \times 10^{-4} \text{ poise in the c g s system})$$
$$= 20\ g\ cm^{-4}\ sec^{-1}$$

This value applies to a tube with an internal diameter of 2 8 mm and a length of 15 cm Given a laminar flow, the product becomes

$$C_{lung\ stat} \times (R_{airway} + R_{tube}) = 0\,005 \times (30 + 20) = 0\,25\ sec$$

This means that, given an abrupt increase in ventilation pressure, the alveolar pressure follows 63% of this pressure after 0 25 sec (this 63% was the starting-point of the calculation, a value of 95% is attained in 0 50 sec)

In the clinical setting the time required is somewhat longer because the ventilation pressure does not increase abruptly but shows a certain slope Moreover, turbulence occurs in the endotracheal tube, and the resistance is therefore more proportionate to r^{-5} This observation warrants the conclusion that, when a 14 French or 16 French tube is used, an inspiratory time of 1 sec is sufficient to ensure adequate transport of gas to and from the alveoli

Apart from the effects of the anaesthetic technique on pulmonary mechanics, the anaesthetic agents used exert an influence on respiration during anaesthesia Of the volatilized anaesthetics, halothane has a marked 'depressant' effect on respiration Devine et al (1958) demonstrated in adults that, upon an increase of the inhaled halothane concentration from 0 4 vol % to 1 5 vol %, the respiratory rate increased significantly while the tidal volume showed a significant decrease This resulted in a virtually unchanged minute volume However, due to the small tidal volume the alveolar ventilation so diminished that a significant reduction of the CO_2 output occurred These investigators also demonstrated that inhalation of 5% CO_2 during deep halothane anaesthesia caused no significant increase in minute volume This implies a reduced sensitivity of the respiratory centre to CO_2 It was also found (Bloch 1966) that the nitrous oxide used in nearly every anaesthesia enhances this effect of halothane Bloch found that addition of N_2O to a concentration of over 70% to an anaesthetic mixture of 0 5-2 0% halothane in oxygen, caused a decrease in tidal volume and an increase in respiratory rate, the minute volume usually showed a marked decrease In view of these findings Bloch advised that a concentration of 70% nitrous oxide should not be exceeded Moreover, even without addition of other anaesthetics N_2O has been demonstrated to have a depressant effect on respiration in infants (Smalhout 1967)

Many anaesthetics, on the other hand, are capable of activating the vagal stretch and deflation endings in the lungs Using the reduced silver stain according to Cajal, Elftman (1943) visualized a wide variety of visceral afferent parasympathetic nerve endings in all parts of the respiratory tract in young dogs No parasympathetic nerve endings were found in the blood vessels The nerve endings in the alveoli were coiled or straight In the alveolar duct they were flattened, and in the bronchiolar wall they were coarse and encapsulated Elftman thought that, due to inflation of the lungs, afferent impulses can form in these structures, and that endings of different morphological aspect can respond to identical stimuli

As early as 1889, Head found that every inspiratory movement inhibits the respiratory centre through the vagus nerve, stimulated by expansion of the lungs Inflation of the lungs causes the respiratory movements to cease, whereas marked collapse of the lungs leads to contraction of the diaphragm In order to be able to study the role of the diaphragm independent of the mechanical influence of lung movements, he dissected flaps of diaphragm in rabbits, using a transabdominal approach This method has since been adopted by other investigators According to Head, the inhibitory effect on the respiratory centre is such that discharge of the respiratory centre is prevented by elevation of the 'discharge threshold' In this way, he believed, the potential energy of the centre is at the same time maintained at a certain level The inhibitory effect can also produce an increase in respiratory rate in that the discharge periods are shortened so that recovery of the potential energy is accelerated Severance of the vagus nerve branches results in an increase of

inspiratory tonus, but this effect disappears after some time when, according to Head (1889b), the centre becomes exhausted

Considerable research has been done by dissecting vagus nerve fibres and recording action potentials from them under various conditions

Adrian (1933) was the first to study the reflexive inhibitory influence of inspiration by examining the impulses in isolated afferent fibres He found that certain discharges occurred, not due to movements of the lungs but due to the heart rhythm and the structures near the hilus which are immediately affected by pulsations of the heart and the large vessels The true stretch receptors in the lungs resemble muscle spindles in that they only slowly adapt themselves to the stimulus by deformation, that is to say distention of the tissue in which they are localized The frequency of the action potentials depends on the degree of inflation of the lungs, and the discharge continues virtually undiminished if the lungs are kept in a certain state of inflation for some time Marked deflation of the lungs effected by suction of air, likewise gives rise to action potentials During normal lung movements, however, these do not occur The function of the stretch receptors is to 'scan' the volume of the lungs at any moment, and inhibit the stimulus which causes distention Adrian agreed with Head that these receptors exert their inhibitory influence on the respiratory centre chiefly by elevating the discharge threshold, and 'not by preventing the accumulation of active material'

Paintal (1955, 1957) was able to localize the deflation receptors in a pharmacological study, making use of the fact that these receptors are intensively stimulated by phenyldiguanide The interval between injection and discharge was shortest upon injection of this substance into the bifurcation of the pulmonary artery, no discharge occurred upon injection into the left ventricle According to Paintal, the deflation receptors are probably localized near the alveoli He argued that the deflation receptors described by Adrian are not the true deflation receptors because a heart rhythm was present in the impulses derived from them

Insufflation of the lungs with ether, trichlorethylene and chloroform stimulates and sensitizes the deflation receptors Paintal defined this sensitizing as that effect of a substance on a receptor that lowers the absolute threshold to the physiological stimulus

Whitteridge and Bulbring (1944) and Whitteridge (1958) reported that trichlorethylene, ether, nitrous oxide, cyclopropane and halothane cause an increase of the rate of discharge in dissected vagus nerve fibres This effect occurs in rapid as well as in slow inflation of the lungs, and is therefore not solely dependent on the rate of inflation When high concentrations of these anaesthetics are given, however, the initial stimulant effect is followed by paralysis except in the case of nitrous oxide or cyclopropane However, Whitteridge (1958) believed that this paralytic effect on the stretch receptors will not occur at the maintenance concentrations used in clinical anaesthesia

The abovementioned findings do imply, meanwhile, that the volatilized and

gaseous anaesthetics conventionally employed in clinical anaesthesia so influence the proprioceptive control of respiration as to give rise to a type of respiration characterized by a increased respiratory rate, b smaller tidal volume, c increased state of contraction of the diaphragm with increased functional residual capacity even during the expiratory phase The characteristics a and b were clearly demonstrated for halothane by Devine et al (1958)

C Respiration in infants with internal hydrocephalus

In our clinic, increased intracranial pressure is assumed to exist if the intraventricular pressure exceeds 20 cm H_2O (normal value 10-12 cm H_2O) This pressure is determined by means of ventricular puncture through the anterior fontanelle Other accepted indications of increased intracranial pressure are dehiscent cranial sutures and an increase in cranial circumference by more than 1 cm per week If pneumoencephalography discloses that the thickness of the pallium exceeds 3 cm, then surgery is not indicated (Lie 1970) In most cases of lumbar myelomeningocele, internal hydrocephalus develops as well

The question may be raised whether respiration in patients to be treated by a Spitz Holter operation will be more markedly influenced by the anaesthesia than that in patients to be treated for lesser anomalies such as an inguinal hernia or cleft palate Lunn (1968a) found a diminished minute volume during light oxygen/nitrous oxide/halothane anaesthesia in such infants The question of a difference in susceptibility to anaesthetics between 'normal' patients and hydrocephalics can be answered only by comparing the two groups under anaesthesia We have been unable to make such a comparative study, and in the literature we found hardly any data on respiration in infants with hydrocephalus Wylie and Churchill Davidson (1960) made mention of a slow and shallow respiration in association with an acute or severe increase in intracranial pressure Cook (1959) mentioned increased intracranial pressure as a cause of respiratory insufficiency, however, he also stated that in an infant breathing room air and showing no cyanosis, the Pa_{O_2} is probably not significantly increased The fact remains that interpretation of the phenomenon of cyanosis is highly subjective (Comroe and Botelho 1947)

Many of our patients are in excellent clinical condition and show no signs of preoperative respiratory insufficiency In order nevertheless to gain an impression of the gas exchange, we had a preoperative acid base determination carried out in capillary blood from infants to be treated by a Spitz Holter procedure The results are presented in table II

The mean value obtained for the Pa_{O_2} proved to be in agreement with the values reported by Cook et al (1957) and Albert and Winters (1966) But the SD was greater than that found by Albert and Winters (1966) Our series also shows that

Table II Preoperative acid-base state in a number of patients with internal hydrocephalus, determined from capillary blood.

Patient No	Weight (kg)	pH act	pH stand	Bic stand (meq/l)	Base excess (meq/l)	Pa_{CO_2} (mm Hg)	Particulars
70/0067	5.9	7.48	7.51	32.0	+ 8.0	44	– – – –
70/6548	6.1	7.50	7.38	23.0	– 1.0	26	marked hydroc
70/6490	3.1	7.49	7.38	23.5	– 1.0	27	– – – –
70/5761	4.3	7.48	7.41	25.0	+ 1.0	32	– – – –
70/7320	3.8	7.44	7.42	25.0	+ 1.0	37	– – – –
70/7964	3.2	7.42	7.39	24.0	– 0.5	35	– – – –
70/8494	4.7	7.48	7.35	21.0	– 4.0	24	marked hydroc
70/8074	4.0	7.39	7.37	23.0	– 2.0	38	marked hydroc
70/8696	7.7	7.53	7.44	27.0	+ 3.0	29	marked hydroc
70/9433	6.7	7.44	7.38	23.0	– 1.0	32	– – – –
70/9001	6.0	7.43	7.35	22.0	– 3.0	29	– – – –
mean		7.46	7.40		+ 0.5	33	
SD		± 0.04	± 0.015		± 3.0	± 7	

patients with marked hydrocephalus can nevertheless have a normal Pa_{CO_2}. This means that the starting-point of alveolar ventilation in our group of hydrocephalics is the same as that in normal infants; however, this does not warrant the conclusion that the depressant effect of anaesthesia on respiration is necessarily also the same.

D Data from the literature on the influence of anaesthesia and controlled ventilation on cardiopulmonary function

1 INFLUENCE OF ANAESTHETICS, MUSCLE RELAXANTS AND ARTERIAL CARBON DIOXIDE PRESSURE ON CARDIAC OUTPUT

Many anaesthetics have a depressant effect on the contractility of the myocardium. Administration of even small doses of ether, cyclopropane and thiopentone to canine heart-lung preparations exerts a pronounced depressant influence on the myocardium (Wylie and Churchill-Davidson 1960). These authors maintain that, in clinical anaesthesia, a decrease in cardiac output invariably occurs after a certain time. Stephen and Little (1961) reported on the marked depressant effect of halothane on the myocardium, establishing a positive correlation with the concentration of halothane administered. Administration of thiopentone can likewise cause a marked decrease in cardiac output (Prys-Roberts et al. 1967).

Administration of nitrous oxide to test subjects during a steady-state oxygen/halothane anaesthesia causes a significant rise in right atrial pressure, systemic

vascular resistance and forearm vascular resistance The venous forearm compliance diminishes, and the central venous blood volume increases, cardiac output and stroke volume, however, show no significant change (Ty Smith et al 1970) These investigators concluded that both nitrous oxide and cyclopropane have a sympathomimetic effect which to some extent antagonizes the sympatholytic effect of halothane

Relaxant drugs can likewise influence the circulation Galindo and Davis (1962) reported that succinylcholine has a sympathetic postganglionic stimulant effect, combined with a direct effect on the myocardium Its administration by intravenous drip for over an hour in monkeys produced a fall of the cardiac excitability threshold and a change in myocardial contractility force, independent of changes in blood pressure Development of hypertension and tachycardia following administration of a large dose of succinylcholine also indicates postganglionic stimulation, particularly since this effect is enhanced by blocking the preganglionic efferents by total spinal anaesthesia These authors consider direct stimulation of the adrenal glands by succinylcholine possible as well Churchill-Davidson (1970) likewise held that succinylcholine, like acetylcholine, can have a direct effect on the myocardium through stimulation of the sino-auricular node Aoyagi and Piiper (1965) found that an intravenous dose of 2 mg succinylcholine produced an increase in arterial pressure, heart rate, cardiac output and effective right atrial filling pressure in dogs This indicates a pronounced sympathomimetic effect in these animals

On the other hand, many investigators have pointed out the vagotonic effects of succinylcholine Ieri et al (1965) held that it can directly stimulate the vagal motor centres According to Beretervide (1955), succinylcholine competes with acetylcholine for true cholinesterase, as a result, newly synthetized acetylcholine accumulates This increases central nervous parasympathetic activity with, as a result, bradycardia and hypotension Williams et al (1961) found that ganglionic blocking by means of trimetaphan prevents the circulatory responses to succinylcholine This, too, suggests that they are mediated via sympathetic and parasympathetic nerves Positive pressure ventilation did not affect the bradycardia produced by succinylcholine

Children in particular are susceptible to parasympathomimetic effects Leigh et al (1957) repeatedly observed marked bradycardia with transient circulatory depression in children The bradycardia was manifested in the ECG by a decelerated sinus rhythm or a nodal rhythm In some cases there were signs of ectopic atrial innervation The use of ether in anaesthesia prevents these vagotonic effects of succinylcholine, as Williams et al (1961) later confirmed Bush (1964) pointed out that burned children can show cardiac arrest after administration of succinylcholine Perhaps the vagal effects are potentiated by the acidosis frequently present in burned children Meyer and Hugin (1963) mentioned ventricular fibrillation in a 14-year old patient after a second dose of succinylcholine Repeated administration of succinylcholine is frequently a cause of bradycardia and hypotension (Williams

et al 1961, Dentan and Vourc'h 1967) Mathias et al (1970) found that, in adults, this bradycardia can be prevented by prophylactic administration of a non polarizing muscle relaxant in quantities up to 25% or less of the muscle relaxant level They explained the phenomenon by assuming that the succinylcholine stimulates afferent vagal receptors such as the carotid sinus baroreceptors This reflex is blocked by non-polarizing muscle relaxants According to Craythorne et al (1960) intramuscular succinylcholine administration causes no bradycardia in children, possibly due to the slow absorption

In clinical anaesthesia, the parasympathomimetic and sympathomimetic effects of succinylcholine, combined with mechanical irritations such as endotracheal intubation, giving rise to reflexive vagal or sympathetic discharges, produce several changes in cardiac rhythm tachycardia, bradycardia and ectopic beats of varying origin According to Smith (1967), severe cardiac instability rarely occurs if sufficient atropine is given prophylactically, if it is administered during vagal stimulation, however, marked arrhythmias can occur

The $Pa_{(O_2}$ has been found also to influence cardiac output Prys-Roberts et al (1967) found that the cardiac output diminished to 72% of the value in spontaneous respiration if the $Pa_{(O_2}$ was decreased to 23 mm Hg They studied 19 anaesthetized patients without cardiovascular and pulmonary abnormalities In hypercapnia ($Pa_{(O_2}$ = 80 3 mm Hg) the cardiac output increased The relationship they established between cardiac output and $Pa_{(O_2}$ was $\dot{Q}$ (1/min/70 kg) = 0 039 $Pa_{(O_2}$ (mm Hg) + 2 23 Morgan et al (1967) found a decrease in cardiac output by 9% at a $Pa_{(O_2}$ of 20 mm Hg, and an increase by 36% with a rise in $Pa_{(O_2}$ from 40 to 60 mm Hg They obtained their findings by ventilating dogs and measuring the flow in the superior vena cava and descending aorta with the aid of ultrasonic flow transducers Theye (1966) likewise mentioned the influence of hypocapnia on cardiac output An increase in cardiac output as a result of hypercapnia was prevented in dogs with the aid of the β-receptor blocker practolol (Norman et al 1970) In this respect we may note that $Pa_{(O_2}$ values of 20, 60 and 80 mm Hg are unusual in clinical anaesthesia Given a decrease in $Pa_{(O_2}$ from 40 to 25 mm Hg, a decrease in cardiac output by about 16% is to be expected on the basis of the equation of Prys-Roberts et al

2 INFLUENCE OF SPONTANEOUS RESPIRATION AND CONTROLLED VENTILATION ON CARDIAC OUTPUT

a The heart as a pressure-suction pump

Purkinje (1843) observed that, with a closed pericardium, the apex shows relatively little displacement during systole The atrioventricular ring, however, is drawn towards the apex during systole This is why Purkinje described the apex as 'punctum fixum', and the atrioventricular ring as 'punctum mobile' This observation was confirmed by Rollet in 1880, he found that, whereas the ventricle empties upon the downward movement of the atrioventricular ring, the atria are filling (more and

more) with blood. Rollet concluded from this finding that the flow of blood from the veins to the heart is accelerated during systole. At fluoroscopic examination of a patient with calcified mitral valves, Böhme (1936) observed that the calcified ring pulsated in a direction opposite to the movements at the apex. In cats injected with large amounts of thorotrast, he observed acceleration of the blood flow in both superior and inferior vena cava during ventricular systole. The systole was accompanied by reduction of the ventricle, enlargement of the atrium and reduction of the calibre of the inferior and superior vena cava. The author consequently assumed that blood is drawn from the vena cava to the atrium during systole.

Brecher (1956) described the effect of the heart action per sé on venous return. With Hubay, he used flow meters for simultaneous determination of the blood flow rates in superior vena cava and pulmonary artery in dogs. The flow of blood to the right atrium proved to be largest when the tricuspid valves were closed during ventricular systole (no communication between atrium and ventricle). The flow curve of the superior vena cava showed two peaks: a high one during systole and closed tricuspid valves, and a lower one during diastole. Moreover, the flow proved to stop or even reverse itself in the event of an isolated atrial contraction occurring at 2:1 or 3:1 block.

With the pericardium open, the apex of the heart is less firmly fixed, and the descent of the atrioventricular ring is less evident. In this case the blood flow rate in the superior vena cava proves to be diminished during systole. Simultaneous registration of the blood flow in superior vena cava and pulmonary artery (Brecher and Hubay 1955) has demonstrated that the flow acceleration in the two vessels is simultaneous: 'The two tracings fit into each other like finger and glove, making it easy to conceive the heart as a pressure-suction pump'.

b *The respiratory pump*

In the preface to Brecher's book 'Venous Return' (1956), Wiggers wrote: 'It is axiomatic that the heart can pump only as much blood as it receives'. The amount received is so largely dependent on respiration as to warrant the designation 'respiratory pump'. However, the effect largely depends on the amount of blood available in the lungs and in the central venous system (see below). This blood store enables the circulation to adapt itself quickly to changing conditions, e.g. an abruptly increased oxygen requirement of the tissues, or some impairment of the heart action.

In a report published in 1826, Barry described the results of experiments in horses and dogs in which he studied the influence of respiration on the blood flow in the jugular vein. Like Donders (1853a), he pointed out that the physiologist Albrecht von Haller had established a correlation between respiration and venous blood flow rate as early as 1760: during inspiration, he had observed that the jugular vein, subclavian veins and superior vena cava emptied themselves towards the heart and collapsed. 'But the mechanism was never printed out, by which nature,

in these animals, applies the mighty agency of atmospheric pressure to the veins, and connects, as cause and effect, the expansion of the chest with the afflux of the centripetal fluids to the heart' Barry described how he observed in horses and dogs that, during the expiratory phase, the external jugular vein distended, while it immediately collapsed during the inspiratory phase In one of his experiments, he replaced a segment of the left jugular vein of a horse by a bulbed glass tube In the recumbent and quietly breathing animal, he then observed acceleration of the blood flow through the bulb, synchronized to the chest expansion From this observation he concluded that the blood is sucked towards the chest cavity during inspiration, and that atmospheric pressure is the propellant force In the standing horse, there was no correlation between respiratory movements and blood flow pulsations occurred at a rate exceeding that of the arterial pulse The blood flow rate was determined for the most part by the law of gravity The pulsations described by Barry show a marked similarity to the collapse phenomena later described by Holt (1941, 1943)

Donders (1853a) believed that, as a result of the subatmospheric pressure in the thorax, venous blood is continuously being sucked towards the chest cavity even during the expiratory phase The flow in the inferior vena cava is likewise promoted by respiration during inspiration, the blood is not only sucked into the thoracic cavity but also pressed from the abdominal cavity by the then increased intra abdominal pressure According to Donders, the circulation in the liver is also greatly favoured because the hepatic veins open up into the thoracic segment of the inferior vena cava The view that the blood flow rate to the thorax increases more or less in proportion to the force of the inspiratory movement is the so-called 'classical theory of Donders'

Donders (1853b) also observed that, 'bei hohem Ausatmungsdrucke mit abge schlossenen Luftwegen', the pulse diminishes and sometimes disappears, while the heart sounds become feeble and sometimes are no longer audible Due to the high intrathoracic pressure, only little blood is still flowing to the heart And even this is impaired during diastole

However, Holt (1941, 1943) demonstrated that the large veins do not behave as rigid tubes He let dogs breathe in a pressure chamber in which the pressure could be varied from +20 to −20 cm H_2O As the chamber pressure was increased, auricular pressure and femoral venous pressure likewise increased A decrease in chamber pressure resulted in a decrease in auricular pressure, but the pressure in the femoral vein showed no further decrease once the chamber pressure had attained a certain subatmospheric value This means that a collapse state must have occurred somewhere in the venous system Holt verified his hypothesis in a test model a system of tubes in which a certain segment consisted of jugular vein When the pressure gradient between the ends of the tube system increased, the flow also increased After a certain pressure gradient, however, the flow showed no further increase and the jugular vein showed partial collapse The flow then assumed a pulsating

character The effect of the pulsating flow was demonstrated in live dogs by Brecher (1952a) Holt further observed that, in a test subject breathing in a pressure chamber, the peripheral venous pressure in the abducted arm did not decrease below a certain value when the chamber pressure came below a certain limit

Holt assumed that the partial collapse occurs immediately before the passage of the brachiocervical trunk into the chest cavity Duomarco and Rimini (1954) characterized the venous system as a system of collapsible tubes, taking their course through various body compartments which, by their characteristic properties, exert an influence on the system The chest cavity can be compared to a gas filled space in which a subatmospheric pressure prevails, and which is separated from other spaces by the chest wall and the diaphragm The abdominal cavity can be compared to a fluid-filled space This fluid has the same density as blood The space is traversed by the flaccid inferior vena cava These authors found a small pressure gradient along the jugular vein in live dogs Immediately after the passage into the chest cavity, a single steep fall in pressure occurs at this point there is a collapse of the jugular vein The pressure gradient along the superior vena cava as far as the heart, is gradual again The pressure gradient in the abdomen along the inferior vena cava as far as the diaphragm, is small As the diaphragm is passed, a marked fall occurs The gradient along the intrathoracic segment of the inferior vena cava is small again Auricular pulsations are visible in the pressure curve of the superior vena cava, but these are not conducted to the jugular vein and inferior vena cava Nor is this the case with the pressure variations resulting from respiration Only during the expiratory phase can the peaks of the central venous pulse become visible in the jugular vein and inferior vena cava Respiratory variations in venous return to the heart are therefore regarded by these investigators as the result of slight impediments during the expiratory phase, and they conclude that a decrease in intrathoracic pressure during inspiration cannot cause an increase in the flow of blood to the thorax as a result of collapse Brecher (1956) disagreed with this conclusion He maintained that determination of pressure gradients alone, without measuring flow as well, yields insufficient information to warrant such a conclusion

According to Brecher (1952a), Donders' 'classical theory' and Holt's and Duomarco and Rimini's 'collapse theory' are not controversial but complementary As long as collapse does not (yet) occur during inspiration, Donders' theory applies The collapse phase, with the possible occurrence of high frequency oscillations of the blood flow, does not occur until a subatmospheric blood pressure of -10 cm H_2O is attained This is unthinkable during normal spontaneous respiration The phase preceding the collapse phase was called 'depletion phase' by Brecher In this context, collapse is to be defined as the change from a circular to an elliptic cross section of a vein There is a phase of transition between non-collapsed intrathoracic veins and collapsed extrathoracic veins (Brecher et al 1952b)

The collapsibility of the veins entering the chest cavity protects the right heart against overfilling upon deep inspiration or upon the pronounced blood suction

which occurs in the Muller test (inspiration with closed glottis) Another physiologically important consequence is that the collapsibility, together with the blood storage function attributed to the large veins, permits of an increase in the minute volume of the heart without a decrease in venous pressure In this way the venous blood store ensures an uninterrupted flow of blood to the right heart This has its counterpart in the air-chamber function of the aorta and arterioles, which convert the intermittent ejections of blood from the left ventricle to continuous tissue perfusion (Brecher 1956)

Sjostrand (1953) pointed out that the amount of blood in the thoracic organs also fulfils an important store function The amount of blood in the lung capillaries is not large 90 ml in a resting adult (Forster 1959) It increases during active exercise and decreases in response to a Valsalva manoeuvre The store blood in the lungs is contained in sinus-like vessels localized between the elastic and collagenous structures of the pulmonary tissue (Sjostrand 1953) These connect the lung capillaries with large pulmonary veins According to Sjostrand, 30% of the total blood volume is contained in the thorax, of the intrathoracic blood, some 75% is localized in the lungs, and the remainder is contained in the heart This store of blood ensures rapid adaptation whenever a disproportion develops between the blood supply to the heart and the cardiac output The store blood in the lungs then determines the rate at which the left heart can fill during diastole and, therefore, the maximum stroke volume and minute volume During anaesthesia there is displacement of blood from the pulmonary to the systemic circulation If the amount of intrathoracic blood decreases to less than 15% of the total blood volume, then the cardiac output becomes directly dependent on fluctuations in venous return

Such investigators as Brecher, Hubay, Mixter and Share have used direct flow measurements to study the venous return to the heart and the flow in the pulmonary artery in dogs in various experimental arrangements With the chest closed, the venous return through the superior vena cava during the inspiratory phase increases for the duration of the depletion phase A slight decrease occurs during expiration The flow in the superior vena cava is always larger during normal respiration than in respiratory arrest (Brecher and Mixter 1953a) These authors established that the effects were less evident in test animals suffering from hypovolaemia With the chest opened, contraction of the respiratory musculature exerts no influence on the flow in the superior vena cava

The situation with regard to the inferior vena cava is more complicated Duomarco and Rimini (1954) explained to which influence this vein is subject in its intra-abdominal and intrathoracic course Mixter (1953) made flow measurements in dogs by placing Pitot flow meters in the abdominal and in the thoracic segment of the inferior vena cava At the same time he recorded the intra abdominal and intrathoracic pressures (during inspiration, the former increases and the latter decreases) The flow in the intrathoracic inferior vena cava increases while that in the abdominal segment hardly changes The pressure in the femoral vein, however,

increases somewhat This suggests partial collapse of the inferior vena cava Due to contributions from the hepatic veins and the renal venous system, the flow in the thoracic segment of the inferior vena cava always exceeds that in its abdominal segment Severance of the phrenic nerve and its accessories eliminates the diaphragm, in which case the intra-abdominal pressure decreases during inspiration, while the pressure in the femoral vein does the same This indicates facilitated drainage of blood through the abdominal inferior vena cava The flow increases correspondingly With the chest opened, contraction of the diaphragm causes an increased flow in the thoracic inferior vena cava because the blood is expelled from the abdominal segment of this vein

Gollwitzer Meier (1932) reported that, particularly in chiefly thoracic breathing, the return of blood through the abdominal inferior vena cava and the portal system is favoured during inspiration and impaired during expiration Dependent on the type of respiration, however, the reverse is not uncommon

c Influence of controlled ventilation on cardiac output

Numerous investigators have observed that controlled ventilation of test subjects and test animals results in a decrease in cardiac output As pointed out, this decrease results on the one hand from a decrease in Pa_{O_2} due to hyperventilation, but on the other hand is caused by mechanical factors Beecher et al (1943), for example, observed that an increase of intratracheal pressure in spontaneously breathing dogs reduced the circulation diminished pulse pressure and decreased flow in femoral and carotid arteries Most investigators attach the greatest importance to the influence of ventilation on the venous return It is possible, however, that the ventilation causes a change in the resistance of the pulmonary vascular bed as well

Applying the Fick principle, Cournand et al (1948) studied the influence of three types of IPPV on the cardiac output in test subjects with closed thorax Mixed venous blood was obtained from the pulmonary artery or the right ventricle Ventilation type I was characterized by a symmetrical pressure curve (derived beneath the mask) with a gradual increase and then a gradual decrease in pressure Inspiratory and expiratory phase were of approximately the same duration The end-expiratory pressure remained slightly above the atmospheric Ventilation type II was characterized by rapidly increasing pressure during inspiration, followed by a pressure plateau and subsequent rapid decrease during expiration In this type, too, the end-expiratory pressure slightly exceeded the atmospheric, but the inspiratory phase lasted twice as long as the expiratory phase Type III, finally, was characterized by an asymmetrical pressure curve Inspiratory pressure gradually increased but expiratory pressure quickly decreased to atmospheric level The expiratory phase lasted as long as or longer than the inspiratory phase The mean ventilation pressure was lowest in type III and highest in type II

Cournand et al found that the cardiac output diminished in type I and type II ventilation, but showed a slight increase in type III In three patients with therapeutic

pneumothorax, they found a good positive correlation between changes in cardiac output and effective end-diastolic right ventricular filling pressure They maintained that experiments in this type of patients are suitable par excellence to establish this relationship The pressure in a therapeutic pneumothorax is a much closer approximation to the immediately pericardial pressure than are intrathoracic pressures measured in normal subjects (cf Chapter III) Werko (1947) even maintained that conduction of the ventilation pressure to various intrathoracic organs is so variable that it can be held at least partly responsible for the relatively marked variation in the effects of controlled ventilation on the circulation in various patients

The lastmentioned ventilation curve from the publication of Cournand et al (1948) is commonly referred to as 'Cournand type III'

Gordon et al (1956) found that the ideal ventilation curve should meet at least the following requirements a a gradual increase in inspiratory pressure to +20 cm H_2O and an abrupt decrease during the expiratory phase, b rate of ventilation to be adapted to the patient's age 12 cycles/min for adults, and 30-50 cycles/min for infants

Kuyper (1965) determined the cardiac output in dogs according to the Fick principle His study is important because he was the first to obtain measurements in test animals during the steady state He also ensured that the switch from spontaneous respiration to controlled ventilation was made without a change in alveolar ventilation His steady state criteria were constant values during at least 30 min for the parameters $\dot{V}_{O_2}$ $\dot{V}_{(O_2}$, Sa_{O_2}, $S\bar{v}_{O_2}$, pH, $FA_{(O_2}$, pressure in aorta and pulmonary artery, pressure in trachea and oesophagus, body temperature and the electrocardiogram Kuyper established that a decrease in cardiac output occurred during IPPV The $S\bar{v}_{O_2}$ of blood from the pulmonary artery likewise decreased Even ventilation at a mean intratracheal pressure of 0 cm H_2O (as in spontaneous respiration) caused a decrease in cardiac output in dogs (Aoyagi and Piiper 1965) The latter authors relaxed their test animals with the aid of succinylcholine

A decrease in cardiac output and venacaval flow due to IPPV has been reported by other investigators also A decrease in flow in the superior vena cava in dogs during IPPV with closed thorax was demonstrated by direct measurements by Brecher and Mixter (1953a), Hubay et al (1954) and Abel and Woldhausen (1968) The firstmentioned authors observed a distinct decrease in flow due to mild positive pressure lung inflation Deflation of the lungs caused an immediate increase in flow, but evidence of increased left heart output was not seen in the arterial pressure tracings until after three cardiac cycles In comparison with spontaneous respiration, the superior venacaval return to the heart was significantly reduced According to Hubay et al (1954), the effect of positive pressure ventilation on the flow in the superior vena cava is quite marked in the case of hypovolaemia, in such cases an increase in flow can be effected by introducing subatmospheric pressure during the expiratory phase Mixter (1953) reported that positive pressure ventilation reduced

the flow in the thoracic and the abdominal segment of the inferior vena cava, particularly in hypovolaemia (when collapse of the inferior vena cava in the abdomen readily occurs)

According to Glick et al (1969), inflation of the lungs in dogs at a pressure of 27 cm H_2O invariably has a negative inotropic and chronotropic effect, believed to result from activation of the vagal stretch receptors of the lungs The effect can be prevented by bilateral cervical vagotomy Their experiments, however, involve no controlled ventilation but sudden inflations, initiated from the end-expiratory position Whether these phenomena occur in human subjects also remains to be established

3 INFLUENCE OF SPONTANEOUS RESPIRATION AND CONTROLLED VENTILATION ON RESISTANCE IN THE PULMONARY VASCULAR BED

Reduction of the venous return to the heart is regarded as the principal cause of the decrease in cardiac output during IPPV or IPNPV

A more controversial issue is the influence of respiration and controlled ventilation on resistance in the pulmonary vascular bed According to Tigerstedt (1903), this resistance is very small The circulation can be totally abolished if the lungs are very vigorously inflated through the trachea Abolition of this pressure is followed by reappearance of the pulse wave in the aorta within 0 4 0 7 sec The blood pressure rises within a few seconds De Jager (1879), however, demonstrated that the degree of distension of the lungs influences the resistance in the pulmonary vascular bed the rate of perfusion through isolated porcine and canine lungs increases when these lungs are expanded from a collapsed state in a vessel in which negative pressure is induced

Brecher and Hubay (1955) simultaneously determined the flow in the superior vena cava and in the pulmonary artery, the flow in the latter vessel was observed also to increase during inspiration, but always one heart beat later This flow reaches a maximum when that in the superior vena cava begins to diminish Effective pressure and resistance in the pulmonary artery likewise increase during inspiration They concluded from these findings that, in spontaneously breathing subjects, the resistance in the pulmonary vascular bed shows a slight increase during inspiration Others, however, have doubted the correctness of this conclusion (Linde et al 1961)

Measuring flow rates, Hubay, Brecher and Clement (1955) observed an increase in pulmonary vascular resistance during IPPV in test animals with an open thorax In their experimental set-up, they regarded this increase in resistance as more important than the extracirculatory mechanical factors (they measured the flow in the pulmonary artery twice once while the blood flow was guided through the lungs, and once while it was diverted through a bypass)

Werko (1947) found that IPPV caused only slight changes in pulmonary vascular resistance He, too, regarded the reduction in venous return as the principal cause

of the decrease in cardiac output during IPPV. In a beat-to-beat analysis of the stroke volume, he observed that the stroke volume of the right ventricle diminished during the inspiratory phase, while that of the left ventricle initially increased. The increased intra-alveolar pressure during the inspiratory phase caused blood to flow from the pulmonary vascular bed to the left ventricle. This phenomenon was later confirmed by others (Abel and Woldhausen 1968). We frequently observe it during anaesthesia by means of digital pulse plethysmography: during the final part of the inspiratory phase, the amplitude of the oscillations on the scope is seen to increase. In open-heart surgery, too, the abrupt marked increase in blood flow to the left atrium is quite evident during inspiration.

Proctor and Yamabayashi (1961) demonstrated on the basis of histological findings that even tamponade of lung capillaries is possible. They examined canine lungs fixed with formalin vapour at an intra-alveolar pressure of 25-28 cm H_2O. The small blood vessels seemed compressed, and no capillaries were visible. In specimens prepared at an inflation pressure of 5 cm H_2O, however, adequate capillary filling was visible.

The resistance in the pulmonary vascular bed is therefore in part dependent on lung distension, which in turn is dependent on transpulmonary pressure (Maloney and Whittenberger 1957). As lung distension in increases, the volume of the larger blood vessels and of the bronchi and bronchioles increases due to radial traction of the elastic alveolar walls. Since the periphery of the lungs has a larger surface area than the central structures, the outward forces acting upon the large blood vessels exceed the inward forces (Howell et al. 1961). At a marked increase in transpulmonary pressure, however, the resistance in the small blood vessels can be increased by more than the value of the decrease in resistance in the larger vessels (Simmons et al. 1961). Some authors (Linde et al. 1961; Maloney and Whittenberger 1957) maintain that it is unimportant whether lung distension results from increased intra-alveolar pressure or from decreased peripulmonary pressure. However, the intra-alveolar pressure required to create a certain level of transpulmonary pressure for inflation of the lungs is bound to be higher with a chest wall of low compliance than with a more compliant chest wall. Permutt et al. (1961, 1962) pointed out that, at a high intra-alveolar pressure, the pulmonary vascular resistance is no longer solely dependent on lung distention. As soon as the intra-alveolar pressure exceeds that in the pulmonary veins or the left atrium, the difference between pulmonary artery pressure and intra-alveolar pressure is determinative for the flow in the pulmonary vascular bed. According to Roos et al. (1961), the resistance in IPPV increases as the intrapulmonary pressure increases. However, this influence is less marked in a pressure range of 7-13 cm H_2O than in a range of 17-23 cm H_2O. Given inconsiderable lung inflation, a degree of expansion of the capillaries in fact still takes place; but at higher pressures they are longitudinally stretched.

Werkö (1947), Simmons et al. (1961) and Linde et al. (1961) determined pulmonary vascular resistance by assuming a linear relationship between resistance (R),

cardiac output ($\dot{Q}$), pulmonary artery pressure (PAP) and left atrial pressure (LAP). This gives the equation $R = \frac{PAP - LAP}{\dot{Q}}$. Roos (1962), however, described the reality as a highly complex interaction between: a. the viscous properties of the blood (dependent on haematocrit, diminution with dilatation of a blood vessel); b. turbulence; c. pulsatile driving pressure; d. distensibility of the vascular bed.

Donald (1962) maintained that an increase in transpulmonary pressure to 8-12 cm H_2O exerts little influence on pulmonary vascular resistance.

Since low ventilation pressures are used in clinical anaesthesia, we conclude from these data from the literature that pulmonary vascular resistance is not likely to show marked changes during IPPV, particularly since the compliance of the chest wall in infants is so high that total compliance is in fact determined by that of the lungs. However, we do attach great importance to avoidance of any external pressure on the infant's chest during surgery.

4 INFLUENCE OF CHANGES IN CARDIAC OUTPUT AND VENTILATION ON ARTERIAL BLOOD OXYGENATION

During anaesthesia, the Pa_{O_2} is unfavourably influenced by a number of factors (Nunn 1964; Nunn et al. 1965; Prys-Roberts et al. 1967). Changes in the distribution of ventilation/perfusion ratios, of true shunts and of cardiac output cause an increase of the pulmonary venous admixture. In normal adults, atropine increases the physiological dead space by 8% (Nunn and Bergman 1964); the normal value is about 25% of the tidal volume. Cook et al. (1957) found a value of 32% for infants. From the data supplied by various authors, Nunn et al. (1965) calculated a pulmonary venous admixture of 3.6-6.2% for normal adults. During anaesthesia, this value was 11.3% in spontaneous respiration and 9.3% in controlled ventilation. In spontaneously breathing patients, the Pa_{O_2} is further affected unfavourably by the hypoventilation which always prevails in that case.

The abovementioned authors concluded from these findings that the FI_{O_2} of the anaesthetic gas mixture for spontaneously breathing patients should be 35-40% in order to ensure adequate arterial oxygen pressure. During controlled ventilation, an FI_{O_2} of 30% is sufficient, provided that heart and lungs are normal.

Sykes et al. (1965) likewise found an increased venous admixture, which they ascribed chiefly to a change in the distribution of the pulmonary blood flow as a result of anaesthesia. Atelectasis, they thought, might also play a role in this respect.

The problem of the relationship between cardiac output and amount of shunt blood has been experimentally and theoretically approached by several authors. Of the total amount of blood which reaches the lung from the right ventricle every minute, a certain proportion does not participate in the gas exchange through the alveolar membrane. A proportion of this shunt blood flows through the thebesian system which, according to Ravin et al. (1965), consists of three communicating vascular systems opening up into the left heart: a. arterio-luminal vessels: com-

munications between a small branch of the coronary artery and a heart cavity; b. arterio-sinusoidal vessels: starting as arterioles and emptying into an atrium or ventricle via irregular capillary-like structures; c. the thebesian veins proper: channels between coronary veins or distal ends of capillaries, and the heart cavities. The shunt blood of the thebesian system accounts for about 11% of the total amount of shunt blood.

Verloop (1948) described the anastomoses of the pulmonary vascular system. The bronchial arteries supply the bronchial tree up to and including the bronchioles, as well as the adventitia of the pulmonary vessels and part of the visceral pleura. The pulmonary artery supplies the remainder of the visceral pleura. The bronchial arteries have small branches which anastomose with small lateral branches of the pulmonary artery. Similar anastomoses are found in the visceral pleura; these end in interlobular branches of the pulmonary artery. Most of the venous blood in bronchi and visceral pleura is drained off by branches of the pulmonary vein. Only a small amount of the blood in the largest air passages is carried off by the bronchial veins to the large body veins.

The amount of intrapulmonary shunt blood can vary. It increases in certain pulmonary affections (emphysema), with increasing age and during anaesthesia. The following considerations are derived from various publications by Prys-Roberts, Kelman, Greenbaum and Nunn, which appeared in 1967. Pulmonary venous admixture is defined as the quotient $\dot{Q}s/\dot{Q}t$, in which the numerator is the amount of shunt blood per unit of time, while the denominator is the total cardiac output. The oxygen content of the shunt blood is held to equal that of mixed venous blood. Mixed venous blood results from complete admixture of the venous blood from the body organs: this admixture becomes complete downstream in the pulmonary artery.

If the cardiac output $\dot{Q}t$ diminishes while the body's oxygen consumption remains constant, then the $C\bar{v}_{O_2}$ diminishes. Since the blood flow through the tissues is then slower, more oxygen is withdrawn from it. The shunt blood then likewise has a lower oxygen content. This blood mixes with the blood which did completely participate in the gas exchange; and the result is that the 'mixed' arterial blood has a lower oxygen content than end pulmonary capillary blood. This leads to an increase in gradient A-a P_{O_2}. This gradient depends on: a. the oxygen content of the mixed venous blood, which in turn largely depends on cardiac output (Rahn and Fenn 1955), and b. the percentage of venous admixture. The relationship is quantitatively shown in fig. 4. The position of the isoshunt lines in this figure is determined by PA_{O_2}, oxygen consumption, Hb concentration, acid-base state and temperature of the blood.

Because a physiological shunt is always present, a decrease in Ca_{O_2} as such produces an additional slight decrease in $C\bar{v}_{O_2}$ (Kelman et al. 1967).

Prys-Roberts et al. (1967) found an unmistakable increase in A-a P_{O_2} in association

with a decrease in cardiac output in response to an injection of thiopentone. This difference is also increased by IPPV. In that case, hyperventilation during anaesthesia can cause a paradoxical fall of the Pa_{O_2}. The hyperventilation reduces the PA_{CO_2} and increases the PA_{O_2}. The decrease in cardiac output caused by controlled ventilation and hyperventilation and anaesthetics, however, causes an increase in gradient A-a P_{O_2}. The resultant for the Pa_{O_2} is in part dependent on the percentage of pulmonary venous admixture (fig 5).

If in spontaneously breathing test subjects one increases the FI_{O_2} from 47% to 99.5%, then the PA_{O_2} rises from 290 to 655 mm Hg. A decrease in gradient A-aP_{O_2} then occurs (Cole and Bishop 1963); according to these authors, the pulmonary artery shunts are indeed oxygenated at this high PA_{O_2}.

According to Rees (1950), the oxygen concentration of the gas mixture used in IPPV of infants during anaesthesia should be at least 50% because hyperventilation causes a shift to the left of the Hb dissociation curve, which impairs the supply of oxygen to the tissues.

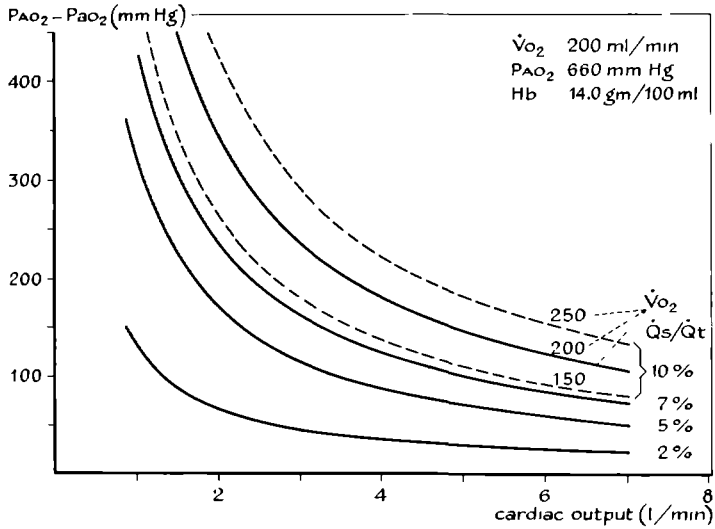

Fig. 4 Mathematical model of the relationship between alveolararterial P_{O_2} difference, cardiac output and pulmonary venous admixture. The 'iso-shunt' lines are calculated for the parameters shown in the top right hand corner of the diagram

Reproduced from Prys-Roberts, C., Kelman, G. R., and Greenbaum, R. (1967) *Anaesthesia* 22, 257 By kind permission of the publishers

E Summary of this chapter

According to the literature, the Pa_{O_2} in normal infants is lower than that in adults 25-36 mm Hg Infants therefore have a relatively larger alveolar ventilation Inspiratory movements must overcome the elastic and viscous resistances of the lungs, the resistance of the gas flow and the extrathoracic resistance due to displacement of abdominal contents The lung compliance is determined by the elastic and viscous resistance of the pulmonary tissue This compliance is small in infants as compared to that in adults 5 2-7 9 ml/cm H_2O But the compliance of the chest wall in infants is large 17 2-31 2 ml/cm H_2O The compliance of the respiratory system, therefore, is largely determined by the lung compliance and amounts to 2 8-5 4 ml/cm H_2O The lung compliance diminishes during anaesthesia

The respiratory rate in infants is about 38 cycles/min

The oesophageal pressure amplitude resulting from spontaneous respiration is 5 ⁻ 4 cm H_2O in normal infants These pressure fluctuations also occur as a result of IPPV, but their amplitude is relatively smaller

Respiratory work in adults and infants is in part dependent on respiratory rate

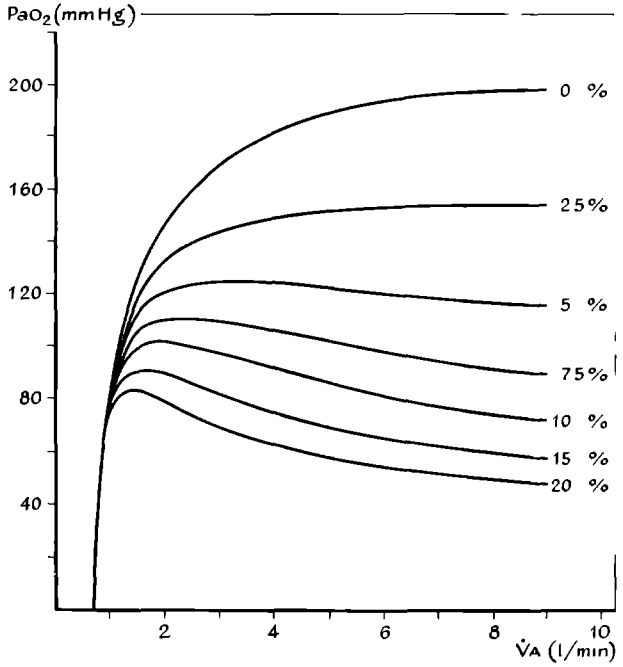

Fig 5 Relationship between arterial P_{O_2} and alveolar ventilation for several values of $\dot{Q}s/\dot{Q}t$ FI_{O_2} –0 3 Reproduced from Kelman G R, Nunn, J F Prys Roberts, C and Greenbaum, R (196⁻) *Brit J Anaesth* 39, 150 By kind permission of the publishers

Although the resistance in the respiratory tract in infants is about 10-15 times that in adults, the amount of respiratory work per square metre of body surface is about the same in adults and infants.

Endotracheal intubation greatly increases the resistance in the respiratory tract in infants. Due to the increased resistance and the effect of gaseous and volatilized anaesthetics, a change in type of respiration occurs: increased respiratory rate, smaller tidal volume and increased functional residual capacity.

To ensure adequate gas transport through the tube in controlled ventilation of infants, an inspiratory and expiratory duration of 0.5-1.0 sec should be chosen.

The preoperative starting-point of the alveolar ventilation was found to be the same in a group of hydrocephalics as in normal infants.

Administration of anaesthetics and a decrease in Pa_{CO_2} due to hyperventilation cause a decrease in cardiac output. Intravenous succinylcholine can produce the same result by parasympathomimetic effects. The latter, however, can be prevented by premedication with an adequate amount of atropine, and by using ether in anaesthesia. IPPV reduces the venous return through the vena cava. Normal respiration favours the venous return (the respiratory pump). The IPPV procedure used influences the degree of decrease in cardiac output. A gradually increasing ventilation pressure during the inspiratory phase, followed by a rapid decrease to atmospheric value during the expiratory phase, exerts the least influence on cardiac output. The expiratory phase should be at least as long as the inspiratory. The ventilation curve thus obtained is known as 'Cournand type III'.

A slight increase in transpulmonary pressure due to controlled ventilation exerts little influence on the resistance in the pulmonary vascular bed.

A decrease in cardiac output and other effects of the anaesthesia lead to an increase in pulmonary venous admixture. As a result, the A-a P_{O_2} gradient increases. It is therefore necessary that anaesthetized patients be offered an FI_{O_2} of 35-40% during spontaneous respiration. An FI_{O_2} of 30% is sufficient during controlled ventilation.

Changes in the oxygen content of mixed venous blood are primarily dependent on changes in cardiac output; changes in the $P\bar{v}_{CO_2}$ depend chiefly on fluctuation in the ventilation.

Personal observations

The category of patients studied has been described in chapter I. All these infants were free from cardiac and pulmonary abnormalities.

The patients were premedicated by intramuscular injection of 0.125 mg (sometimes 0.25 mg) atropine 30-60 min before induction of anaesthesia. The anaesthesia was given by means of a Rees system. This consists of a T-piece according to Ayre (1937); to its expiratory part (length about 10'), Rees (1950) attached a balloon for manually controlled ventilation. In the modern model the expiratory part consists of a flexible tube of corrugated rubber (fig. 6).

Fig. 6: The Rees anaesthesia system. 1. supply of fresh gas; 2. endotracheal tube; 3. expiratory part; 4. ventilation balloon.

For induction of anaesthesia we used a gas mixture of 2 l oxygen and 3 l nitrous oxide to which volatilized ether, penthrane and halothane had been added. As soon as the depth of anaesthesia permitted it, the patients were intubated with a 16 French reinforced tube. In some cases we had to use a smaller size (14 French). Unless this is specifically stated, no muscle relaxant was used in intubation. After intubation, anaesthesia was continued with 2 l oxygen, 3 l nitrous oxide, ether and penthrane. Since the surgeon infiltrates the skin of the field of operation with a local anaesthetic containing adrenaline (1:100,000), we considered the use of halothane in continued anaesthesia to be unjustifiable in view of the possible occurrence of multifocal ventricular tachycardias (Brindle et al. 1957).

The following parameters were studied in our cases.

1 BLOOD SAMPLES FROM THE RIGHT ATRIUM

These samples were obtained through the atrial drain which the surgeon had placed in situ The correct position was established electrocardiographically For this purpose the drain was filled and intermittently flushed with a 3% NaCl solution Postoperatively, the position was always verified by radiological examination The oxygen saturation and acid-base state of the samples were determined In all cases, at least two samples were taken, namely

a from the spontaneously breathing patient, as soon as the drain had been placed in situ,

b 1-2 min after the patient had been relaxed with 4 mg succinylcholine (0 5-1 5 mg/kg body weight) through the intracardiac drain and received IPPV

In view of the acid-base state results, and taking into account that many of the infants in this study were kept fasting for hours owing to the intricacies of the operation schedules, we selected 13 patients for a study of the effect on the acid-base state of a 10% glucose solution given by continuous drip through a gastric catheter, starting 3 hours after the last feeding and continuing until induction of anaesthesia Infants younger than 10 days were not given glucose The dosage was as follows Body weight 3-4 kg 15 ml/hour, 4-5 kg 20 ml/hour, 5-6 kg 25 ml/hour, 6-7 kg 30 ml/hour, over 7 kg 40 ml/hour In this manner we bridged intervals of, in some cases, 7 hours The patients of this group received controlled ventilation throughout the anaesthesia Before anaesthesia was induced, the gastric catheter was removed and at the same time an attempt was made to drain off such fluid as was still contained in the stomach

The blood samples were drawn up into heparinized Luer Lock syringes through the drain, fluid was drawn up into the syringe until unmistakable blood appeared This mixture of heparin, saline solution and blood was then discarded, whereupon 3 ml blood was drawn up as a sample All samples were examined immediately

The acid-base state was determined according to Åstrup, with the aid of a Radiometer set pH meter 27, tonometer AMT-1 and micro-electrode G297/G2 The 6% and 10% CO_2 mixtures required for equilibration were continuously prepared by means of gas mixing pumps from the component pure gases CO_2 and air

The oxygen saturation of the haemoglobin was determined by the spectrophotometric method of Siggaard-Andersen et al (1962) the blood is centrifuged off in heparinized capillaries and haemolysed in the HEM - I haemolyser (Radiometer), the oxygen saturation is determined in the oxygen saturation meter OSM - I (Radiometer) These determinations were made in the Clinical Chemistry Laboratory of our hospital

2 OESOPHAGEAL PRESSURE

In a number of patients we measured the changes in oesophageal pressure which occur at the switch-over from spontaneous respiration to IPPV after succinyl-

choline relaxation. After induction of anaesthesia, a latex oesophageal balloon on a polyethylene catheter was passed into the middle one-third of the oesophagus. The length of the balloon was 2.5 cm; the catheter segment contained within the balloon had a number of small lateral perforations. The oesophageal balloon was connected up with a combined pressure amplifier and transducer: the Godard p-amplifier. This in turn was linked to a Hellige Multiscriptor 9400/4. The system was filled with 0.2-0.3 ml air. The mean pressure amplitudes and the mean change in mean oesophageal pressure were calculated from the oesophagograms (the latter values by means of planimetric integration).

During the recording of oesophagograms it was repeatedly found that succinylcholine administration was followed by such a change in oesophageal pressure that an adequate ventilation oesophagogram on the recorder could be obtained only if the p-amplifier was so adjusted that the read-out for end-expiratory pressure during IPPV roughly corresponded again with the end-expiratory pressure during spontaneous respiration.

In 11 patients, therefore, we tried to establish how exactly the end-expiratory oesophageal pressure behaves if: a. spontaneous respiration is replaced by IPPV after succinylcholine relaxation; b. ventilation is then briefly stopped; c. spontaneous respiration has been resumed; d. succinylcholine is again administered.

In all these ventilation experiments we were unable to use a random sequence because: a. the duration of the effect of an intravenous dose of succinylcholine varies, and in the interest of the patient the experiment should not too much affect the duration of the operation; b. after succinylcholine injection there is no return to the initial condition as soon as the spontaneous respiration seems to be sufficient again in view of the pressure amplitude on the oesophagogram.

In 6 relaxed patients, finally, we determined the degree of conduction of a static intratracheal pressure to the oesophagus. We established how the oesophageal pressure changed upon application of static intratracheal pressures of 0, 5, 10, 15 and 20 cm H_2O (in these experiments, the resistance encountered by the gas flow in the air passages plays no role).

3 RIGHT ATRIAL PRESSURE

In a number of patients we recorded oesophageal pressure and atrial pressure simultaneously with the aid of a Dupo FM 410 pressure transducer/amplifier system connected to the Hellige recorder. By means of a polyethylene catheter filled with a heparinized 0.9% NaCl solution, the transducer was connected to the cardiac drain as soon as this was in situ. As point of reference for the atrial pressure we chose the mid-axillary line. The table with the patient was first adjusted to the appropriate height, whereupon the transducer was adjusted at the level of the reference point. We assumed that the adjustment was correct if three persons agreed that it was. We always ensured that the height of the table was not changed once the height of the transducer was adjusted.

Muscle relaxation was achieved in all cases by injection of 4 mg succinylcholine through the intracardiac drain, combined with an intramuscular injection of the same dose To prevent cardiac arrhythmias, another intramuscular injection of 0 125 mg atropine was given before induction of anaesthesia The mean atrial pressure was indicated by the Dupo amplifier by means of electrical integration The change in effective right atrial filling pressure after the switch-over from spontaneous respiration to IPPV was determined by subtracting the mean oesophageal pressure change from the mean atrial pressure change within the same time interval

All pressure determinations and calculations of pressure curves were carried out by the Department of Medical Physics, where also the curves obtained were independently evaluated as to their validity in the context of this study In 13 cases the curves obtained were of sufficient quality for calculation, this group included 6 patients in whom we studied the question whether, during spontaneous respiration and subsequent IPPV, mean oesophageal pressure and atrial pressure are sufficiently constant over somewhat longer periods to warrant the conclusion that changes which occur after the switch-over to IPPV, can indeed be attributed to this switch-over

The frequency characteristics of the system used to measure the right atrial pressure were determined with the aid of a pressure generator (Vierhout 1966) The resonance frequency of the system atrial catheter – polyethylene catheter – Dupo transducer/amplifier proved to be 16 Hz The resonance frequency of the transducer/amplifier without catheters exceeded that of the Hellige recorder (> 50 Hz) In the low frequency range, therefore, the frequency characteristics of the entire system were determined by the catheters

Taking into account the non-sinusoidal a, c and v peaks, we estimate the frequency of an atrial pressure curve at a heart rate of 150 beats/min to be about 10 Hz, and a fair reproduction can therefore be expected Vierhout (1966) reported a frequency of 0-12 Hz for children, and of 0-6 Hz for adults It should be pointed out, however, that the frequency characteristics are of no importance for determination of the mean right atrial pressure

To determine the significance of a difference in the statistical analysis of results, we made use of the formula

$$n > \left(\frac{3\,242\sigma}{\delta} \right)^2,$$

in which n is the number of observations required to demonstrate a mean (pressure) difference δ with 90% certainty at a level of significance of 5% (two-tailed test), provided that the (pressure) differences show a normal distribution with the same standard deviation (σ)

The experimental set-up is schematized in fig 7, and the sequence of events is shown in fig 8

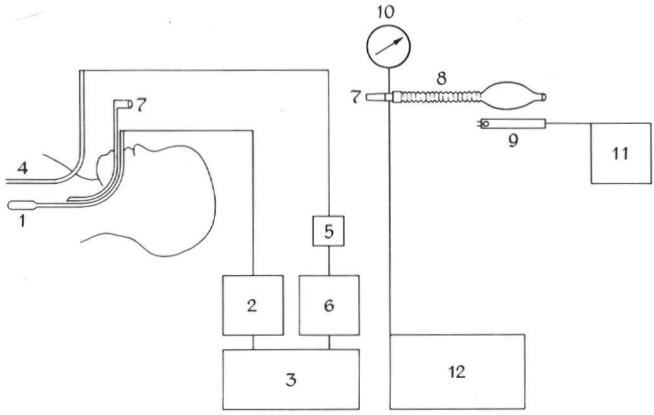

Fig. 7: Experimental set-up. 1. oesophageal balloon; 2. Godard transducer and amplifier; 3. Hellige multiscriptor; 4. right atrial drain; 5. Dupo transducer; 6. Dupo amplifier; 7. endotracheal tube; 8. Rees system; 9. electromechanical thumb; 10. manometer; 11. Sheffield Infant Ventilator; 12. anaesthesia apparatus.

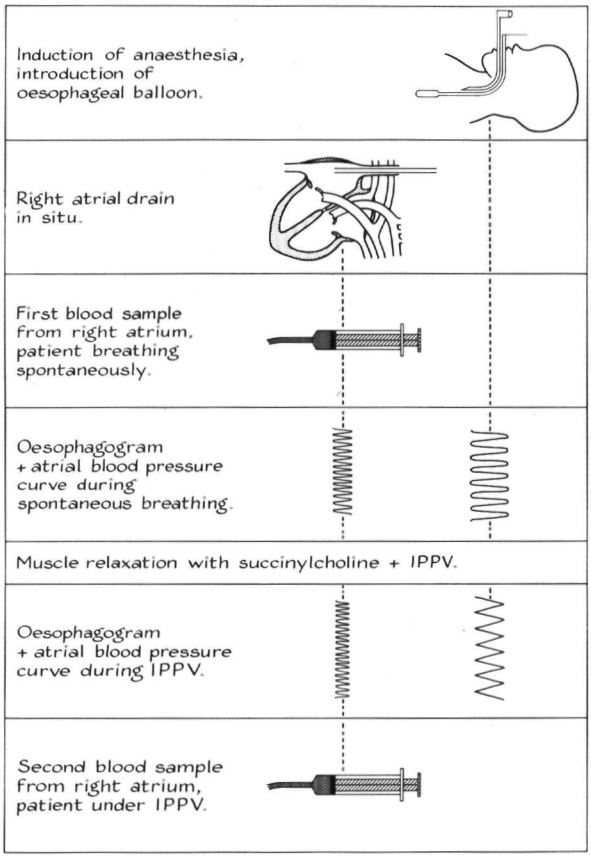

Fig. 8: Sequence of events in 13 patients.

For the IPPV in recording oesophagograms and atrial pressure curves, and for the ventilation of most of the other patients, we employed the Sheffield Infant Ventilator (J. F. Eardley Ltd, Sheffield, England). When the SIV was used, the balloon of the Rees system was replaced by the electromagnetic thumb (fig. 9). In principle, the SIV consists of a Rees system; but opposite the inlet through which the anaesthetic gas from an anaesthesia apparatus flows into the system, there is a branch to a manometer from which the pressure can be read that is built up before the proximal end of the endotracheal tube.

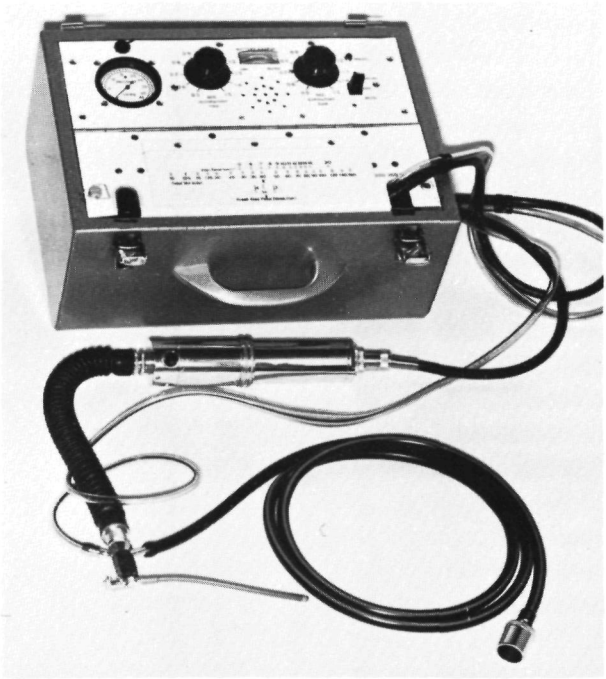

Fig. 9. The Sheffield Infant Ventilator (SIV).

The small diameter of the endotracheal tubes used made it impossible to measure the ventilation pressure past the distal end of the tube. Calibration tests showed that the accuracy of the manometer reading (in cm H_2O) was 100%. The electronic part of the SIV comprises a battery which can be used if no alternating current source is available. The duration of the inspiratory phase and that of the expiratory phase can be independently adjusted. A power transmission cable connects the electronic part with the electromagnetic thumb. The inspiratory phase is induced when the thumb closes the Rees system, so that the in-flowing gas mixture cannot escape from the anaesthesia-patient system. The expiratory phase is characterized by escape of the gas through lateral perforations in the thumb. The inspiratory pressure is therefore determined by: a. duration of closure; b. gas flow rate; c. volume and

compliance of the system-patient combination. In the relaxed patient, therefore, expiration is quite passive. During the expiratory phase it is impossible to create a subatmospheric pressure at the proximal end of the endotracheal tube. The SIV gives an acoustic alarm signal if adequate function of the thumb ceases due to a power failure or exhaustion of the battery. According to Griffiths (1967), the SIV produces an airway pressure pattern which corresponds to the Cournand type III curve.

During controlled ventilation we made efforts to ensure a maximum inspiratory pressure of 20 cm H_2O if possible. This value is usually attained or exceeded in manually controlled ventilation with a Rees system. As ratio between inspiratory and expiratory phase we chose 1:1, at a respiratory rate of 30 cycles/min. The ventilation pressure was then adjusted by adjusting the gas flow to more or less than 5 l/min, keeping the FI_{O_2} constant at 40%.

As we mentioned, we used 16 French reinforced latex tubes (Rusch) for intubation (internal diameter 3.0 mm; length 15.3 cm). Occasionally we had to use a 14 French tube. The pressure-flow characteristics of these tubes were constructed with the aid of a Godard p-amplifier (fig. 10).

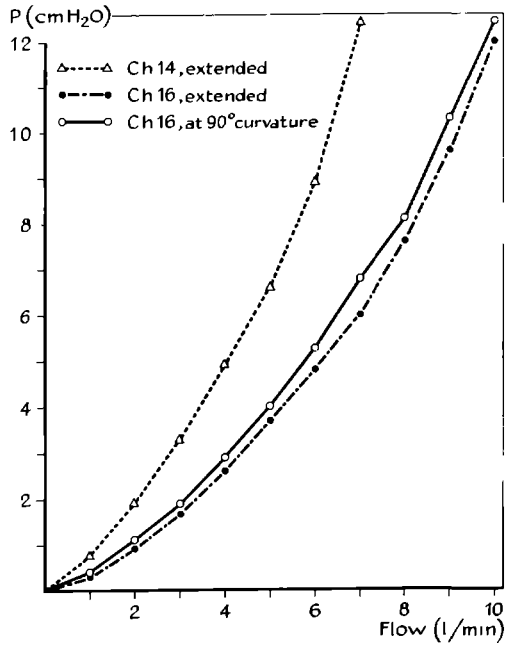

Fig 10 Pressure-flow characteristics of the 14 French and 16 French endotracheal tubes used in this study. All measurements were made with extended tubes, but with the 16 French tube also at 90° curvature, which causes the pressure gradient to increase (by less than 0.5 cm H_2O at a flow of less than 6 l/min). For a continuous flow of less than 5 l/min, the resistance ($R = \frac{P}{\dot{V}}$) is less than 0.8 cm H_2O/l/min

Data from the literature on the parameters used in the personal observations

In chapter I we have listed the determinations we made for the purpose of this study. The present chapter discusses the value which may be attached to these determinations.

1 BLOOD SAMPLES FROM THE RIGHT ATRIUM

Some investigators regard these samples as representative of true mixed venous blood in clinical studies. By definition, this blood is a homogeneous mixture of blood from all parts and organs of the body, with the exception of the lungs. Barrat Boyes and Wood (1957) maintained that admixture of blood flows from the superior vena cava and the coronary sinus is not complete until the blood reaches the pulmonary artery. This is why in many animal experiments blood is taken from this artery for determination of the oxygen content of the mixed venous blood. Catheterization of the pulmonary artery in the clinical context usually poses considerable technical problems; and it can cause cardiac arrhythmias. According to many investigators, however, blood from the pulmonary artery is highly similar in oxygen content to blood from the right ventricle and from the right atrium (Werkö 1947; Theye 1965; Theye and Tuohy 1965). The lastmentioned investigators admitted that determinations of the oxygen content in blood samples from the right atrium may give variable results, but believed that this variability need not be one-sided as long as frequent random samples from the atrium are examined. They considered examination of blood from the right atrium for clinical research purposes in anaesthesiology to be quite acceptable.

The significance of the oxygen content of mixed venous blood for the 'oxygen system' (Theye 1965) of the body can be expressed by writing the Fick equation as:

$$C\bar{v}_{O_2} = Ca_{O_2} - \frac{\dot{V}_{O_2}}{\dot{Q}t}$$

This equation indicates the influence of a change in cardiac output on the $C\bar{v}_{O_2}$ if the oxygen consumption remains constant.

According to calculations based on data supplied by Albritton (1952), over 99% of the total amount of oxygen in mixed venous blood is bound to haemoglobin. According to Sykes et al. (1970) this value is even slightly higher because the oxygen capacity can be assumed to be 1.39 ml O_2 instead of 1.36 ml O_2 per gramme of haemoglobin. Changes in oxygen saturation therefore imply similar changes in oxygen content. In our study, therefore, we have confined ourselves to determinations of oxygen saturation (routine in our clinic) rather than of oxygen content.

Our interest in the behaviour of the oxygen saturation of blood from the right atrium was prompted by the consideration that it might diminish if the cardiac output diminished after the switch-over from spontaneous respiration to IPPV. Rahn and Fenn (1955) held that changes in the oxygen tension of mixed venous blood are primarily dependent on cardiac output and relatively independent of the ventilation. Initially it also seemed possible to us that the oxygen saturation might increase if, with the switch-over to IPPV, the respiratory work would so diminish that the decrease in oxygen consumption would exceed that in cardiac output. Today, however, this assumption seems less plausible to us because we have found that oxygen consumption in dogs does not significantly change upon the switch-over from spontaneous respiration to IPPV. For this purpose we analysed the data on oxygen consumption presented by Kuyper (1965) in his thesis (a mean decrease of 7 ± 22 ml O_2/min proved to occur, which is not significant). Our study, however, provides no complete certainty on this point. This could only be obtained by determining oxygen consumption in our patients before and after the switch-over to IPPV. But since our patients are not in a steady state (cf Section 4), this determination is not meaningful under our test conditions. According to Pfeifer et al. (1962), the energy required for respiration demands about 3% of the basal metabolism in infants. In endotracheal intubation this value might be doubled. Reynolds and Etsten (1966) also found high respiratory work values in intubated infants during anaesthesia. This work, however, was done by controlled ventilation rather than by the patients' respiratory musculature.

The acid-base state was also examined in the blood samples from the right atrium. Rahn and Fenn (1955) found the $P\bar{v}_{CO_2}$ to be primarily dependent on ventilation, and relatively independent of cardiac output. Zahn and Weil (1966) found a close correlation in pH and P_{CO_2} between central venous blood obtained from superior vena cava or right atrium, and arterial blood. They concluded that data on the acid-base state of central venous blood are sufficiently instructive to be evaluated independently: they need not be 'translated' into data on arterial blood. Phillips and Peretz (1969) found that these determinations were of value only as screening procedures. Changes of a metabolic nature are fairly accurately reflected by the venous blood. But they found no sufficient correlation between respiratory alkalosis or acidosis of venous and arterial blood. In our study we have concurred with Rahn and Fenn (1955) in interpreting differences in P_{CO_2} between successive blood samples from the right atrium as resulting from changed ventilation. To the metabolic components we have attached the same significance as we would to those obtained from determinations in arterial or capillary blood.

2 OESOPHAGEAL PRESSURE

Since a decrease in oxygen saturation of blood from the right atrium is indicative of a decrease in cardiac output, it is of importance in our context to involve other parameters which can support this. Because an increase in intrathoracic pressure

results in a decrease in venous return to the right heart, it is of importance to know how the intrathoracic pressure changes after the switch-over from spontaneous respiration to IPPV

The intrathoracic pressure is not the same at all intrathoracic sites The venous return is influenced primarily by pressure changes in the region of the right heart Coleridge and Linden (1954) found that the pressure in the right medial pleural space is most representative of the pressure in the mediastinum enclosing the right atrium The topography of this part of the pleural 'cavity' is most closely related to that of the right atrium These investigators demonstrated in experiments on dogs that the differences between pressures measured in the mediastinum and the right medial pleural space are smaller than those between medial and lateral pleural space The intrapleural pressure, therefore, is not the same at all sites The pressure in the lateral pleural space is usually more subatmospheric than that in the medial pleural space However, Wiggers et al (1947) found that determination of the pressure in the right lateral pleural space in dogs gives very acceptable results for calculation of the effective atrial filling pressure (= pressure measured in the right atrium — intrapleural pressure) In view of the adequate conduction of the pleural pressure to the oesophagus, Von Neergaard and Wirz (1927) thought that the differences in pressure between left and right pleural cavity cannot be large

According to Donleben (1959), the concept of transpulmonary pressure (Comroe et al 1955) should be theoretically defined as the difference between intra-oral or intratracheal pressure and the integrated pressure value at all sites of the lung surface The latter value, however, cannot be experimentally measured An additional practical difficulty is that determinations of intrapleural pressure are of course not feasible in clinical studies of infants

Many investigators believe, however, that determination and recording of changes in oesophageal pressure ensures adequate insight into intrapleural pressure changes (Buytendijk 1949, Mead et al 1955) During spontaneous respiration the oesophageal pressure curve parallels the intrapleural pressure curve Differential determination of these pressures during quiet spontaneous respiration with normal volumes produces a horizontal line At larger respiratory volumes, changes occur the changes in oesophageal and intrapleural pressure are no longer equally marked (Cherniak et al 1955) The lastmentioned investigators therefore advocated a measure of prudence in the interpretation of results of oesophageal pressure determinations, also because in their opinion there is a fair degree of individual variability in the correlation between intraoesophageal and intrapleural pressure Given also the findings of Coleridge and Linden (1954) and the topography of the oesophagus in the mediastinum, determination of changes in oesophageal pressure and recording of oesophagograms (Buytendijk 1949) is a clinically valid and not too inconveniencing method of investigation for the determination of changes in intrathoracic pressure According to Donleben (1959), the results are in fact a better approximation of the medial pleural pressure than the lateral pleural pressure

Determinations of oesophageal pressure can be influenced by a number of factors Buytendijk (1949) described the artefacts which become visible due to oesophageal contractions The influence of the heart action is as a rule visible in oesophagograms This phenomenon is explained by the close topographic relationship between the oesophagus on the one hand, and the heart with aortic arch and descending aorta on the other Because of this relationship, Tondury (1949) differentiates between an upper pars retrotrachealis and a lower pars retropericardiaca (or inter-aorta-azygos) of the oesophagus Benjamins (1914) introduced an oesophageal catheter at the level of the atrium or the ventricle, and simultaneously recorded an oesophagogram and an ECG Thus he observed atrial waves immediately after the P peak and ventricular waves after the QRS complex Mead and Whittenberger (1953) found the phenomenon to be maximal in the distal one-third of the oesophagus

The elastic properties of the oesophagus likewise play a role in this respect The oesophagus is normally collapsed Inflation of an oesophageal balloon with air means insufflation of the oesophagus itself An amount of air which causes no increase of pressure in an oesophageal balloon outside the oesophagus, does produce such an increase when the balloon is inside the oesophagus (Mead and Whittenberger 1953) The amount of air in the balloon, therefore, should be kept as small as possible – also with a view to the response time of the system used to determine the oesophageal pressure (Mead and Whittenberger 1953)

The proper situation of the balloon in the oesophagus is a controversial subject Wawersik (1967) placed it in the distal one-third of the oesophagus, as did Barnes et al (1969) In our opinion it is a disadvantage of this method that, in infants, the balloon is easily pushed past the diaphragm unless it is introduced under fluoroscopic control Some authors merely mention that the balloon is placed in the intrathoracic part of the oesophagus In 7 normal adult test subjects, Milic-Emili et al (1964) investigated the influence of the balloon localization on the intraoesophageal pressure measured In the upper part of the oesophagus, the pressure proved to depend in part on the position of the head and on external pressure upon the trachea At lower levels these artefacts are absent, but in the distal one third the pressure is partly dependent on the position of the body (dorsal recumbency, lateral recumbency, etc) The middle one-third of the oesophagus, however, is virtually free from all these influences The pressure measured at this level is most representative of the local pleural pressure This is why Lunn (1968b) placed the oesophageal balloon in the middle one-third of the oesophagus in his abovementioned studies in infants It was here that he, too, found the greatest pressure changes as a result of respiration

The findings reported by Milic-Emili and Lunn prompted us to place the oesophageal balloon in the middle one-third of the oesophagus whenever possible in our study

Most investigators make use of small air filled balloons in studying infants Cook et al (1957) used water filled catheters, but they considered it probable that the other method is more sensitive

The inconsiderable lung compliance, in combination with the large compliance of the chest wall, causes the intrapleural pressure (with the oesophageal pressure as its representative) to vary much more widely during spontaneous respiration than during IPPV, in which the same transpulmonary pressure is created. In the former case the intrapleural pressure is a 'work pressure' which increases the transpulmonary pressure. In the latter case the intrapleural pressure is a secondary value: in that case the work pressure is provided by the ventilation system which induces an increase of pressure in the airway. The intrapleural (or oesophageal) pressure increase is now dependent on: a. intratracheal pressure; b. lung compliance; c. compliance of the chest wall and extrathoracic organs (abdominal contents). Wawersik (1967) also maintained that less marked pressure variations in the oesophagus must be expected during controlled ventilation than during spontaneous respiration.

3 RIGHT ATRIAL BLOOD PRESSURE

In a number of our patients we recorded the pressure in the right atrium. Several investigators have reported that the effective right atrial filling pressure increases when IPPV is applied (Cournand et al. 1948; Werkö 1947; Aoyagi and Piiper (1965).

The effective right atrial filling pressure is the difference between the mean pressure determined in the atrium and the mean intrapleural (or oesophageal) pressure. The value thus obtained is representative of the effective end-diastolic filling pressure in the right ventricle. This correlates with the degree of stretch of the muscle fibres of the right ventricle at the end of diastole. This stretch is one of the factors which determine the amount of stroke work of the right ventricle (Sarnoff 1955). According to this author, direct determination of the end-diastolic pressure in the ventricle is exceedingly difficult at high heart rates. Determination of the mean atrial pressure is much simpler and has the additional advantage that one can establish whether a valve insufficiency is present, as a result of which blood flows back to the atrium during the ventricular systole. In our study this was indeed observed in one case.

Green (1948) attached little value to atrial pressure as a parameter of cardiac output and venous return. In the large veins and the atria, the amount of blood can increase very substantially without any significant change in atrial pressure. On the other hand, a change in the capacity of the venous store can cause the atrial pressure to change without any change in the amount of blood in the central venous store and the atria or in cardiac output.

According to Landis and Hortenstine (1950), central venous pressure is determined by the interaction of a large number of factors. The vis a tergo exerts an influence through the capillary pressure (25 mm Hg). The vis a fronte exerts an influence through normal frictional resistance, cardiac competence and mechanical obstructions. External pressure (vis a latere) is exerted by intrathoracic and intra-

abdominal pressures and the contractility of veins. A final determinant factor is the ratio between blood volume and vascular volume: the vis a parte interiore. Venous pressure both affects, and is affected by cardiac output. An increase in venous pressure due to controlled ventilation, leads to a reduction of the circulating blood volume by filtration through the vascular wall.

Wiggers et al. (1947) and Brecher and Galletti (1963) have pointed out that it is not quite correct to calculate the effective right atrial filling pressure from the mean atrial pressure. They maintained that a number of so-called Z-points must be determined from the atrial pressure curve, whereupon the corresponding oesophageal pressure values must be subtracted. A Z-point comes immediately after the contraction of the atrium, when ventricular diastole is maximal.

The high heart rates in our patients precluded determination of these Z-points. But since we were concerned with the change in mean pressures after the switch-over from spontaneous respiration to IPPV, we considered this disadvantage to be non-essential for interpretation of our results.

4 STEADY STATE

At the end of this chapter we may point out that our patients were not in a steady state. According to Kuyper (1965) this means that one should wait at least 30 minutes. For oxygen uptake, a steady state is attained within a few minutes, but for carbon dioxide excretion it takes longer (Nunn 1967). According to Rahn and Fenn (1955), the oxygen consumption is more constant than the carbon dioxide excretion during an unsteady state. In cardiological diagnostics, a period of 10 minutes is usually considered to be required to attain a steady state. In our patients, the spontaneous respiration during protracted anaesthesia often changed so markedly as to warrant the conclusion that no steady state existed. Moreover, a decrease in body temperature was often found to be inevitable, and this is another factor precluding a steady state. In addition, mention may be made of the disturbing effect of stimuli resulting from the surgical procedure. Since our study compares parameters during spontaneous respiration with those during controlled ventilation, it could hardly be meaningful to wait for a steady state to ensue for the latter (in so far as this could be attained at all according to the criteria of Kuyper) when it had not previously been present.

Results

1 OXYGEN SATURATION AND ACID BASE STATE OF BLOOD SAMPLES FROM THE RIGHT ATRIUM DURING ANAESTHESIA

Table III presents the values found in blood samples obtained during spontaneous respiration (SR) and during IPPV In the group of 28 patients the mean oxygen saturation diminished from 70 3 ± 17 4% to 65 ± 19 8% In view of the wide range of saturation values within the group, we also calculated the mean *individual* change in oxygen saturation which occurred after switch-over to IPPV, which proved to be a decrease of 4 7 ± 5 5% This is significant for $n > 14$

Using the nomogram according to Thews (1967), we calculated the oxygen pressure from the oxygen saturation measured and the pH act In this way we established a mean individual decrease in oxygen pressure of 4 5 ± 3 9 mm Hg This is significant for $n > 8$ The oxygen pressure in the group averaged 46 1 ± 14 mm Hg during spontaneous respiration and 41 6 ± 14 mm Hg during IPPV

The carbon dioxide pressure in the group fell from 44 3 ± 8 9 mm Hg to 39 9 ± 8 5 mm Hg Again we calculated the mean individual decrease, which was found to be 4 4 ± 5 7 mm Hg This is significant for $n > 18$

The pH act of the patients in this group averaged 7 27 ± 0 07, while the pH stand averaged 7 29 ± 0 04 The BE averaged −6 4 ± 2 6 meq/l

Table III Oxygen saturation values and acid-base state of right atrial blood samples before (first line) and after (second line) switch-over to IPPV

Patient no	Weight (kg)	S_{O_2}%	pH act	pH stand	Base excess (meq/l)	$P_{(O_2}$ (mm Hg)	
66/14142	7 4	63 9	7 26	7 27	− 7 9	42 1	(SR)
		56 0	7 29		− 7 7	38 8	(IPPV)
66/14412	9 5	79 0	7 41	7 36	− 2 6	33 4	
		74 5	7 47		− 2 6	27 7	
66/15401	4 8	87 0	7 32	7 33	− 4 2	41 0	
		84 6	7 34		− 3 9	40 0	
66/10484	5 4	69 5	7 21	7 28	− 7 3	51 2	
		71 0	7 25		− 7 1	45 1	
66/10484	6 1	75 5	7 24	7 30	− 5 8	50 3	
		80 6	7 28		− 6 6	42 1	
66/15896	4 6	30 0	7 13	7 27	− 7 5	64	
		22 2	7 11		− 8 5	68	

Patient no	Weight (kg)	S_{O_2}%	pH act	pH stand	Base excess (meq/l)	P_{CO_2} (mm Hg)
67/1754	17 0	85 7	7 42	7 36	– 2 8	31 7
		80 4	7 43		– 2 7	31 2
67/2000	12 3	47 3	7 34	7 33	– 4 3	38 8
		42 2	7 33		– 4 6	38 6
67/3438	4 5	81 4	7 29	7 23	–10 1	32 0
		75 9	7 26		– 9 7	36 3
67/3723	10 3	83 5	7 35	-	– 2 0	43 6
		81 0	7 38		– 0 4	42 0
67/3783	5 4	60 6	7 25	7 27	– 8 2	41 8
		45 7	7 35		– 6 8	31 9
67/4133	6 7	40 6	7 29	7 25	– 9 3	34 2
		34 2	7 33		– 9 1	29 2
67/3281	2 8	60 6	7 33	7 28	– 7 2	33 7
		52 8	7 34		– 8 6	30 0
67/4525	4 3	73 8	7 21	7 25	– 9 2	46 0
		62 0	7 19		– 9 7	46 7
68/1920	5 6	73 0	7 27	7 31	– 5 0	44 9
		58 7	7 29		– 5 2	41 7
68/3357	4 5	76 4	7 33	7 36	– 2 4	44 1
		66 7	7 38		– 1 8	39 3
68/383	4 8	79 8	7 36	7 30	– 6 1	33 8
		75 0	7 37		– 6 6	35 2
68/382	4 8	61 3	7 12	7 25	– 8 8	63 1
		67 6	7 12		–11 1	57 9
68/3002	4 7	66 4	7 17	7 21	–11 0	44 7
		57 5	7 19		–11 6	40 5
68/4062	2 7	31 3	7 29	7 31	– 4 9	42 6
		18 5	7 35		– 7 7	30 9
68/14621	3 7	87 7	7 31	7 31	– 5 8	40 0
		86 6	7 27		– 6 5	43 0
68/14625	4 1	84 6	7 29	7 33	– 4 4	46 9
		83 4	7 34		– 3 9	40 0
69/920	3 8	47 0	7 26	7 26	– 9 1	40 0
		47 3	7 26		– 7 8	42 0
69/755	3 1	77 2	7 24	7 28	– 7 6	48 8
		68 9	7 29		– 6 6	41 6
69/3971	3 6	90 4	7 26	7 28	– 7 4	44 2
		88 7	7 29		– 7 3	39 3

Patient no	Weight (kg)	S_{O_2}%	pH act	pH stand	Base excess (meq/l)	P_{CO_2} (mm Hg)
69/6954	10 3	89 4	7 17	7 22	−11 0	49 5
		88 8	7 30		−10 1	30 2
69/6868	4 3	84 0	7 22	7 34	− 3 7	60 8
		84 7	7 30		− 4 0	44 8
69/6294	3 5	82 3	7 25	7 33	− 4 3	54 3
		83 4	7 28		− 6 7	42 8
Mean and SD during spontaneous respiration		70 3 ±17 4	7 27 ±0 07	7 29 ±0 04	− 6 4 ± 2 6	44 3 ±8 9
Mean and SD during IPPV		65 7 ±19 8				39 9 ±8 5
Mean individual change and SD		4 7 ± 5 5				4 4 ±5 7
Significance*		n > 14				n > 18

* cf equation on page 46

Table IV Acid-base state in right atrial blood samples from 13 patients given a 10% glucose solution by gastric tube before operation IPPV throughout anaesthesia.

Patient no	Weight (kg)	pH act	pH stand	HCO_3^- stand (meq/l)	Base excess (meq/l)	P_{CO_2} (mm Hg)	10% glucose solution (ml)
69/9941*	4 8	7 53	7 35	21 6	−3 2	22	140
69/10555*	4 9	7 43	7 38	23 4	−1 0	34	120
69/12428*	5 3	7 36	7 32	20 2	−5 0	35	120
69/12514*	3 5	7 46	7 30	19 3	−5 9	24	225
69/11340	7 7	7 35	7 34	21 4	−3 7	38	80
69/13534	4 5	7 38	7 36	22 3	−2 5	37	150
69/12428	7 0	7 35	7 31	19 5	−6 0	33	100
70/1274	4 4	7 38	7 25	17 0	−9 0	25	90
70/2402	3 7	7 35	7 33	20 5	−4 6	35	75
70/2455	3 5	7 52	7 35	21 9	−2 9	23	120
70/3389	3 5	7 34	7 36	22 4	−2 2	43	250
70/4098	2 8	7 55	7 35	21 5	−3 2	21	75
70/4117	4 1	7 56	7 42	25 5	−1 3	25	175
Mean			7 34		−4 5	30	
SD			±0 04		± 2 7	± 7	

* IPPV after relaxation with Alloferin®

The data on the influence of preoperative administration of a glucose solution by gastric tube are summarized in table IV. These data also pertain to blood samples from the right atrium. This group of 13 patients received IPPV throughout anaesthesia. The pH stand. in this group was 7.34 ± 0.04, the difference from the untreated group being significant for $n > 7$. The BE was −4.5 ± 2.7, the difference from the untreated group being significant for $n > 5$.

It may be pointed out that the first four patients listed in table IV received IPPV after relaxation with diallyl-bis-nor-toxiferin. dichlorid (Alloferin®). Although we used what we believed to be small doses (0.165, 0.142, 0.125 and 0.100 mg/kg), respiration remained insufficient for several hours after the operation in all these patients; yet neostigmine was administered and the body temperature did not fall below 35°C. We never encountered these difficulties after succinylcholine relaxation.

2 CHANGES IN OESOPHAGEAL PRESSURE

As we mentioned, the end-expiratory oesophageal pressure was often found to change when IPPV was started after succinylcholine relaxation. Table V presents the results of a study of the relationship between end-expiratory oesophageal pressures before and after succinylcholine relaxation in 11 patients. Determinations were made before the surgical intervention. Succinylcholine was given in doses of 4 mg through a scalp vein. Our findings show that: a. succinylcholine relaxation causes a significant increase in end-expiratory oesophageal pressure by 1.1 cm H_2O; b. discontinuation of IPPV, sometimes with simultaneous cessation of the gas flow,

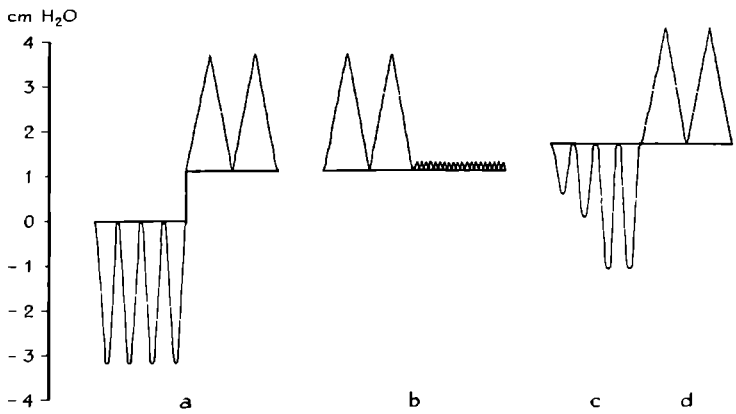

Fig. 11. Schematic representation of the influence of succinylcholine relaxation on end-expiratory oesophageal pressure. The average rise is 1.1 cm H_2O (a). Discontinuation of IPPV does not alter this pressure (b). After resumption of spontaneous respiration the end-expiratory oesophageal pressure remains increased (c). Renewed succinylcholine relaxation no longer significantly influences the pressure (d). The 0-value used was the end-expiratory oesophageal pressure during spontaneous respiration

does not influence this; c. after resumption of spontaneous respiration the end-expiratory oesophageal pressure continues to show a significant increase; d. a second succinylcholine relaxation has no further effect on the end-expiratory oesophageal pressure. Our findings are schematized in fig. 11, while fig. 12 shows a recorded curve.

In a group of 13 patients we recorded oesophagograms before and after starting IPPV following succinylcholine relaxation. The results obtained are summarized in table VI, which shows that the mean pressure amplitude during spontaneous respiration was 3.1 ± 1.7 cm H_2O. During IPPV the pressure amplitude averaged 2.6 ± 0.9 cm H_2O. Including the effect of succinylcholine relaxation on end-expiratory oesophageal pressure, the mean oesophageal pressure rose by 3.2 ± 1.2 cm H_2O when IPPV replaced spontaneous respiration. The mean oesophageal pressure thus reached a significantly higher value ($n > 1$).

Table V Influence of succinylcholine relaxation on the end-expiratory oesophageal pressure

Patient no.	Weight (kg)	ΔP_{oes} I (cm H_2O)	ΔP_{oes} II (cm H_2O)	ΔP_{oes} III (cm H_2O)	ΔP_{oes} IV (cm H_2O)
70/6548	3.6	+0.8	+0.8	+ 1.5	−0 9
70/6490	3.1	−0 8	+0.8	+ 3 2	−0 2
70/6190	3 0	+0.5	+0 5	− 1.0	+ 1 2
70/2338	7.3	0	+0 3	+ 2 5	0
70/0067	5.9	+1 0	+1 0	+ 2 5	0
70/2455	3.5	0	+0.3		
70/3389	3.5	+2.2	+1.7	+ 0.7	+ 2 5
70/4117	3 0	+2 0	+1.7	+ 2.5	+ 0.6
70/0067	4 8	+1.6	−1.6	− 3.7	0
70/2402	3 6	+2.5	−2.5	− 1.0	+ 1 5
70/855	8.6	+1.2	+0 8	0	+ 0.4
Mean		+1.1	+1 1	+ 1.7	− 0.5
SD		±0.8	±0.7	± 1 5	± 1.0
Significance		pos.	pos	pos	neg.
(n)		6	5	9	

Abbreviations

ΔP_{oes} I : Difference between end-expiratory oesophageal pressure during spontaneous respiration and that after relaxation and IPPV.

ΔP_{oes} II : The same, but without IPPV.

ΔP_{oes} III: Difference between initial end-expiratory oesophageal pressure and that after resumption of spontaneous respiration.

ΔP_{oes} IV: Change in end-expiratory oesophageal pressure III upon second succinylcholine relaxation.

The difference between the end-expiratory oesophageal pressures II and III is not significant.

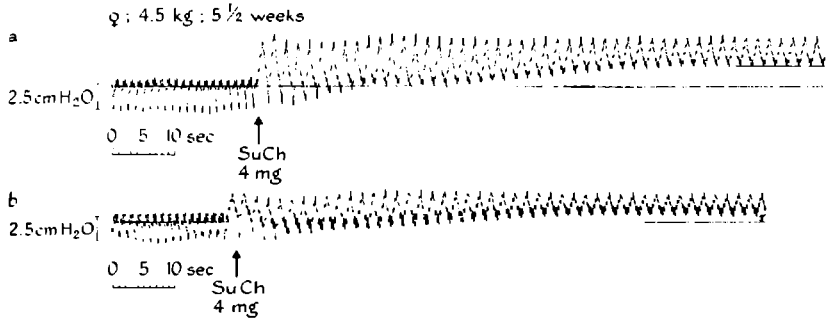

Fig. 12: The influence of relaxation by intravenous injection of 4 mg succinylcholine on end-expiratory oesophageal pressure. In this patient the pressure increases by 2.0 cm H_2O (a), remains constant and, after resumption of spontaneous respiration, is hardly influenced by a second dose of succinylcholine (b).

Table VI: Oesophageal pressure amplitude, mean oesophageal pressure and respiratory rate during spontaneous respiration and after switch-over to IPPV.

Patient no.	Weight (kg)	$\Delta P_{oes}SR$ (cm H_2O)	$\bar{P}_{oes}SR$ (cm H_2O)	SR rate cycles/ min	$\Delta P_{oes}IPPV$ (cm H_2O)	$\bar{P}_{oes}IPPV$ (cm H_2O)	$\Delta(\bar{P}_{oes}IPPV - \bar{P}_{oes}SR)$ (cm H_2O)
68/13916	4.2	0/−3.1	−0.9	46	0/+1.3	+0.9	+1.8
68/13726	4.3	0/−4.9	−0.9	48	0/+3.6	+1.3	+2.2
68/14621	3.7	0/−3.6	−0.9	76	0/+3.6	+1.5	+2.4
68/14625	4.1	0/−2.2	−1.1	48	0/+1.3	+0.4	+1.5
69/920	3.8	0/−2.2	−0.7	35	0/+2.2	+1.0	+1.7
69/755	3.1	0/−4.5	−1.7	37	0/+3.6	+1.8	+3.5
69/3971	3.6	0/−2.2	−1.1	54	0/+3.6	+1.5	+2.6
69/3041	4.8	0/−0.9	−0.1	30	0/+2.7	+0.9	+1.0
69/6954	10.3	0/−1.8	−0.5	55	0/+1.5	+0.5	+1.0
69/6868	4.3	0/−2.2	−0.8	30	0/+3.0	+1.2	+2.0
69/7754	5.5	0/−1.8	−0.5	56	0/+2.0	+0.7	+1.2
69/9043	6.7	0/−7.2	−2.2	28	0/+3.4	+1.4	+3.6
69/8726	3.7	0/−3.6	−1.6	48	0/+1.8	+0.7	+2.3
Mean		0/−3.1	−1.0	45	0/+2.6	+1.1	+2.1
SD		±1.7	±0.5	±14	±0.9	±0.4	±0.9
After correction according to table V							+3.2 ±1.2

Abbreviations

1. $\Delta P_{oes}SR$: Oesophageal pressure amplitude during spontaneous respiration, related to end-expiratory pressure.
2. $\bar{P}_{oes}SR$: Mean oesophageal pressure during spontaneous respiration, related to end-expiratory pressure.
3. $\Delta P_{oes}IPPV$; As 1, but after succinylcholine relaxation and during IPPV.
4. $\bar{P}_{oes}IPPV$: As 2, but during IPPV.

A study of the individual standard deviation of mean oesophageal pressure over a somewhat longer period showed that, in spontaneous respiration and IPPV, this was only 0 1 cm H_2O (patients 69/8726, 69/9043, 69/7754, 69/6868, 69/6954, 69/3041)

The spontaneous respiratory rate showed a considerable standard deviation It amounted to 45 ± 14 cycles/min The respiratory rate during IPPV was set at 30 cycles/min

In two patients (70/7964 and 70/8494) who were relaxed with succinylcholine, we recorded the ventilation curve produced by the SIV (figs 13 and 14), which indeed proved to correspond to Cournand type III

The inspiratory pressure showed a virtually linear increase, while the expiratory phase was characterized by a very steep fall in pressure Given a ventilation pressure amplitude of 20 cm H_2O and an inspiratory and expiratory phase of 1 sec, the mean ventilation pressure before the endotracheal tube was about 6 3 cm H_2O The curves from patient 70/8494 (fig 14) reveal that the ventilation curve produced by the SIV was superior to that produced by the 'trained hand' Ventilation controlled by an 'untrained hand' caused the ventilation pressure to increase substantially, mostly by an increase in end-expiratory pressure Since an interval of about 0 50 sec is required to attain a pressure equilibrium of 95% along the length of the tube (with laminar flow), the mean ventilation pressure in the trachea, distal to the tube, should be slightly less than 6 3 cm H_2O, we estimate this pressure as 6 0 cm H_2O The mean increase in oesophageal pressure in relation to the end-expiratory pressure during ventilation being +1 1 cm H_2O, only 18% of the ventilation pressure is in fact conducted to the oesophagus The small compliance of the lung therefore causes marked subdual of the ventilation pressure

The results of observations in 6 patients in whom the change in oesophageal pressure was determined at static intratracheal pressures of 0, 5, 10, 15 and 20 cm H_2O, respectively, are presented in table VII

The relationship between the two pressures can therefore be written as $P_{oes} = 0\ 23\ P_{trach}$ (approximatively)

Assuming the mean tracheal pressure during spontaneous respiration to be 0 cm H_2O, the change in mean transpulmonary pressure upon switch-over from

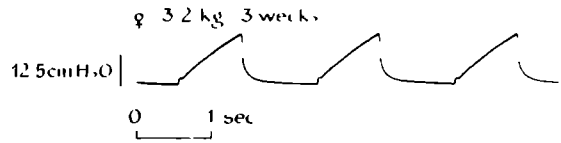

Fig 13 Ventilation curve of the SIV, connected to a patient of 3 2 kg body weight Inflation pressure 20 cm H_2O, duration of inspiratory and expiratory phase 1 sec The inflation pressure shows an almost linear increase During the expiratory phase the pressure shows a very steep fall to the initial value The average ventilation pressure is 6 3 cm H_2O This is a ventilation curve according to Cournand type III

Table VII Relationship between oesophageal pressure and increasing values of static intratracheal pressure

P_{trach} (cm H_2O)	P_{oes} (cm H_2O)
0	0 (initial values)
5	1 2 ± 0 6
10	2 3 ± 0 7
15	3 3 ± 1 0
20	5 1 ± 1 6

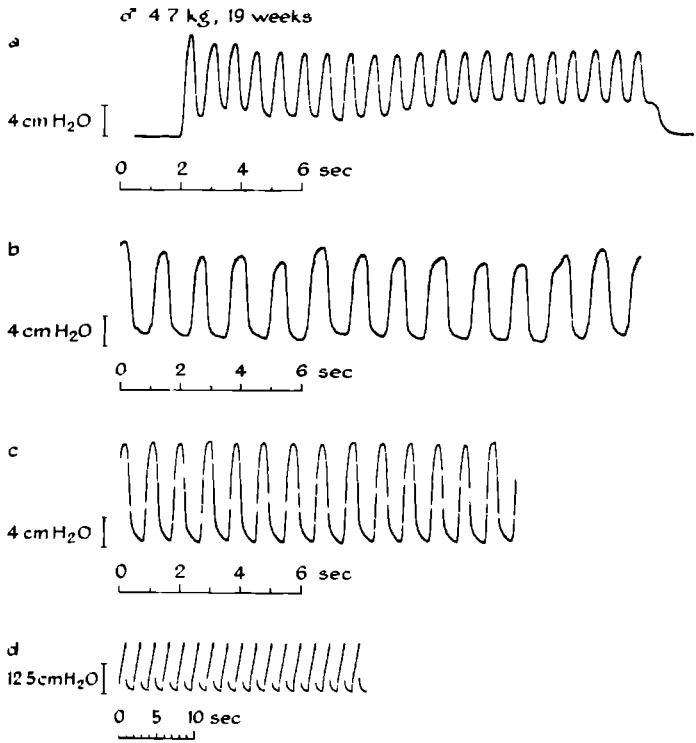

Fig 14a Change in end-expiratory pressure during manually controlled ventilation by an anaesthetic nurse This pressure is not constant

Fig 14b More constant end expiratory pressure during manually controlled ventilation by the same nurse, after instruction

Fig 14c Manually controlled ventilation by the author In order to attain a stable curve, constant alertness is required

Fig 14d Mechanically controlled ventilation gives the most stable curve with the lowest end expiratory pressure

Note The more constant values of the peak inflation pressures of curves a, b and c are due to so sensitive an adjustment of the recorder that the course of the curve became non-linear

spontaneous respiration to IPPV can be written as $\Delta\overline{TPP} = 6 - 3\,2 = +2\,8$ cm H_2O This means an increase of transpulmonary pressure and, therefore, of lung distension When next the IPPV is discontinued, the mean transpulmonary pressure relates to the value during spontaneous respiration as $\Delta\overline{TPP} = 0 - 1\,1 = -1\,1$ cm H_2O This means that lung distension is diminished.

A number of phenomena we have observed in some of our oesophagograms may now be discussed

Patient 68/14621 In fig 15a the amplitude is very constant, but in fig. 15b the situation has changed deep breaths are now followed by several less deep breaths This is identical to the 'Seufzer Atmung' in the capnograms of Smalhout (1967). That the performance is not continuously maximal is demonstrated by the deep sigh (-8 cm H_2O) at the beginning of this period

Patient 69/920 fig 16a shows spontaneous respiration of low respiratory rate and low amplitude During IPPV it was found by coincidence that the end-expiratory level had not changed after succinylcholine relaxation This patient, therefore, certainly required no negative phase in expiration in order to attain the normal end-expiratory level, although respiration was evidently insufficient During spontaneous respiration and IPPV, fluctuations in ventilation pressure were visible in the right atrial pressure curves (fig 16b)

Patient 69/3041 In fig 17a we initially see a respiration with low oesophageal pressure amplitudes, while fig 17b shows the oesophagogram during IPPV after succinylcholine relaxation

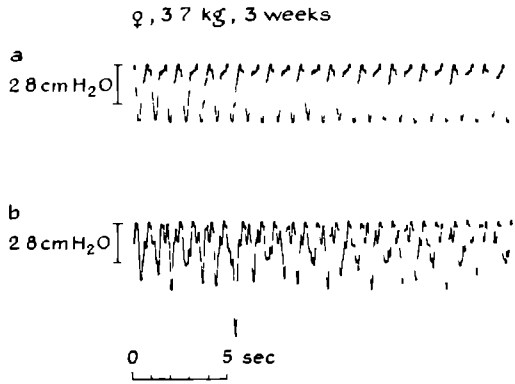

Fig 15a Oesophagogram during spontaneous respiration This is very constant, with a pressure amplitude of 4 2 cm H_2O

Fig 15b The oesophagogram of the same patient 20 minutes later The type of respiration has greatly changed, with pressure amplitude fluctuations of 2 8 4 0 cm H_2O and with an incidental maximum of 8 0 cm H_2O

Patient 69/7754: in fig. 18 it is clearly shown that, during a period of apnoea, the pulsations resulting from the heart action come immediately after the QRS complex. Every pulsation is therefore synchronous with the systole. At a marked increase in intratracheal pressure (+ 15 cm H_2O, static), the amplitude of the pulse waves diminishes.

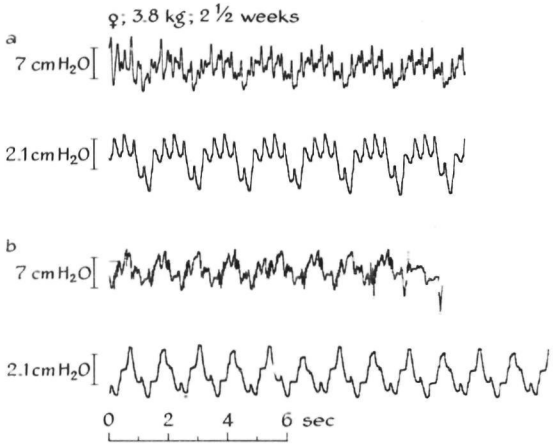

Fig. 16a: Oesophagogram and atrial pressure curve during spontaneous respiration. The oesophageal pressure amplitude is only 2.5 cm H_2O, and the respiratory rate is 35 cycles/min. The atrial pressure curve shows unmistakable respiratory fluctuations.

Fig. 16b: Oesophagogram and atrial pressure curve of the same patient during IPPV. The ventilation pressure is evidently conducted to the right atrium.

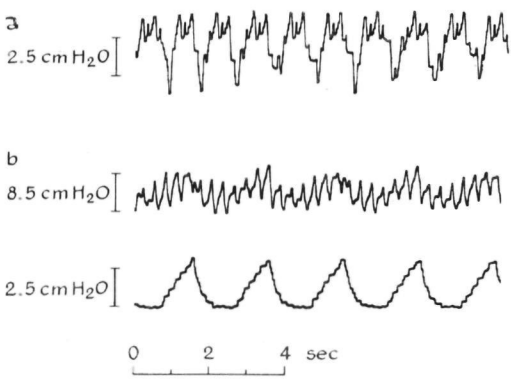

Fig. 17a: Oesophagogram during spontaneous respiration. Pressure amplitudes of 2.5 cm H_2O.

Fig. 17b: Oesophagogram of the same patient after relaxation and IPPV.

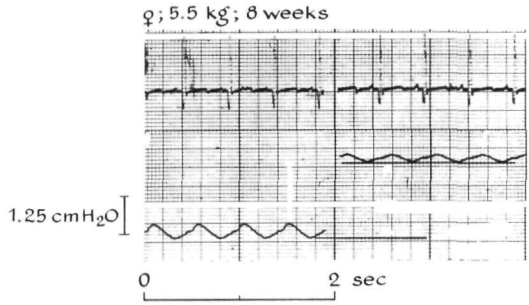

Fig. 18: Change of the conducted pulse waves in the oesophagogram as a result of ventricular systole due to a static rise in intratracheal pressure from 0 to 15 cm H_2O. The pulse amplitude of the oesophagogram diminishes greatly.

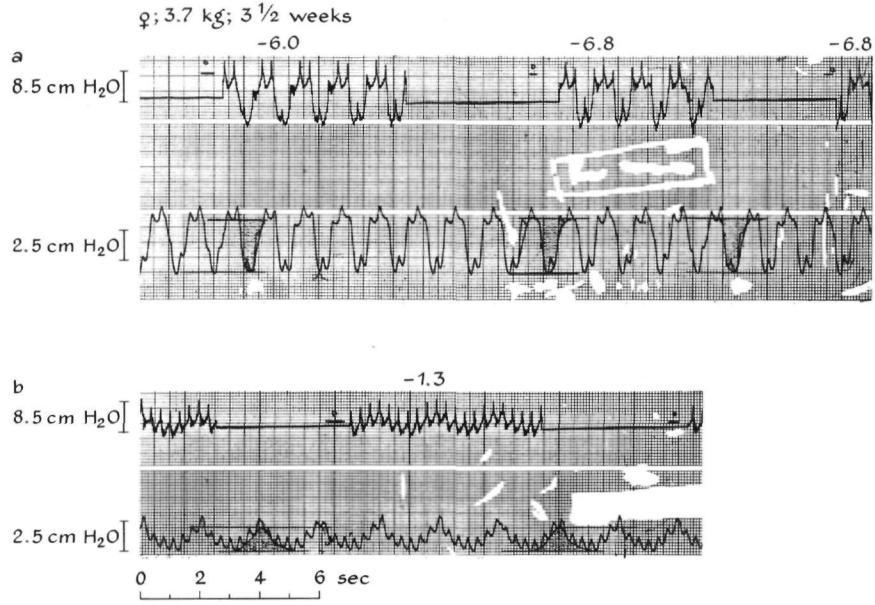

Fig. 19a: Atrial pressure curves and oesophagogram during spontaneous respiration. Read-out of mean atrial pressures and calculation of mean oesophageal pressures by planimetric integration (a). Note stability of mean atrial and oesophageal pressures.

Fig. 19b: Same determinations in the same patient during IPPV. Note stability of mean atrial and oesophageal pressures.

In table VIII we present the results of a study of the stability of the atrial pressure during a number of minutes preceding IPPV and during the period immediately after. This table shows that, during spontaneous respiration, the mean atrial pressure showed an individual variation of 0.5 cm H_2O. The individual variation during IPPV was 0.7 cm H_2O. The method used is exemplified in fig. 19 (patient 69/8726). As we mentioned, the individual standard deviation of the oesophageal pressure in these 6 patients was 0.1 cm H_2O.

Table VIII: Variability of atrial pressure during spontaneous respiration and IPPV.

Patient no.	$\bar{P}_{atr}$SR (cm H_2O)	Variation	$\bar{P}_{atr}$IPPV (cm H_2O)	Variation
69/3041	−0.8[a])	±0.5	−0.3[a])	±1.9
69/6954	+1.2[a])	±0.3	+3.8[a])	±0.6
69/6868	−3.0[a])	±1.2	−0.9[a])	±1.1
69/7754	−5.8[b])	±0.4	+0.8[c])	0
69/9043	−4.8[d])	±0.5	−1.1[e])	±0.1
69/8726	−6.9[f])	±0.1	−1.6[e])	±0.7
Mean variation		±0.5		±0.7

[a]) Mean of two successive mean pressure determinations
[b]) Mean of a series totalling 7 mean pressure determinations.
[c]) Mean of a series totalling 8 mean pressure determinations.
[d]) Mean of a series totalling 12 mean pressure determinations.
[e]) Mean of a series totalling 8 mean pressure determinations.
[f]) Mean of a series totalling 9 mean pressure determinations.

The individual standard deviation of $\bar{P}_{oes}$SR and $\bar{P}_{oes}$IPPV in these patients is 0.1 cm H_2O (page 62).

A change in mean atrial pressure which averages more than 0.5 cm H_2O after the switch-over to IPPV, therefore, is in fact attributable to the switch-over. Table IX shows that the atrial pressure averaged an increase by 3.7 ± 2.1 cm H_2O. From this it can be calculated that the change in mean effective atrial filling pressure was +0.5 ± 2.4 cm H_2O. In view of the large standard deviation, this value is not significant. In our experimental set-up, therefore, the behaviour of the effective atrial filling pressure in response to the switch-over from spontaneous respiration to IPPV was not predictable.

Table IX The change in effective right atrial filling pressure after the switch over from spontaneous respiration to IPPV

Patient no no	$\Delta\bar{P}_{atr}$ IPPV – $\bar{P}_{atr}$ SR (cm H_2O)	$\Delta\bar{P}_{atr}$ IPPV – $\bar{P}_{atr}$ SR (cm H_2O)
68/13916	+1 8	+2 1
68/13726	+2 2	+6 1
68/14621	+2 4	+2 8
68/14625	+1 5	+4 1
69/920	+1 7	+6 7
69/755	+3 5	+4 9
69/3971	+2 6	+0 7
69/3041	+1 0	+0 5
69/6954	+1 0	+2 6
69/6868	+2 0	+2 3
69/7754	+1 2	+6 6
69/9043	+3 6	+3 6
69/8726	+2 3	+5 3
Mean and SD	+2 1 ± 0 9	+3 7 ± 2 1
Corrected	+3 2 ± 1 2	

The mean change in effective atrial filling pressure

$\Delta P_{atr,eff} = (3\ 7 \pm 2\ 1) - (3\ 2 \pm 1\ 2) = +0\ 5 \pm 2\ 4$ cm H_2O

With the aid of a differential manometer, direct determination of the changes in effective atrial filling pressure would have been possible But the advantage of our method was that the quality of the atrial curves could be immediately evaluated In a few instances the method proved to contribute to the localization of the drain in the atrium (when initially this had been passed into the ventricle)

We never observed bradycardia following administration of succinylcholine through the jugular vein The heart rate in fact remained unchanged This means that the acetylcholine effect of the succinylcholine was adequately antagonized by the preceding dose of atropine

Comparison of results obtained with those reported in the literature

1 ACID BASE STATE AND OXYGEN SATURATION OF BLOOD SAMPLES FROM THE RIGHT ATRIUM OF ANAESTHETIZED INFANTS

The values we found for actual and standard pH and for base excess in spontaneously breathing anaesthetized infants (table III) are substantially lower than those found by Albert and Winters (1966) in capillary blood They are also considerably lower than the values we found in hydrocephalics before the operation But the $P_{(O_2}$ values were much higher

Assuming – with Zahn and Weil (1966) and Phillips and Peretz (1969) – that the standard pH of central venous blood is a good indicator of the metabolic component of the patient's acid-base state, we can state that our patients were in a condition of metabolic acidosis The low base excess values also indicate this We believe that a possible cause of this metabolic acidosis is to be found in shivering due to the decrease in body temperature, which we were not always able to prevent However, the fact that our series included cases of marked metabolic acidosis with normal body temperature as well as cases with normal values in spite of a decreased temperature reduces the likelihood of this cause Theoretically, it is also possible that the pH of our blood samples was influenced by contamination with the 3% NaCl solution used by the surgeon to localize the cardiac drain Siggaard-Andersen (1965) reported that dilution of blood with a 10% saline solution caused a decrease in BE and $P_{(O_2}$, whereas the actual pH was hardly affected But the saline solution used in our patients was of much lower concentration, and caused no real dilution of the blood samples The results presented in table IV indicate that the metabolic acidosis can be simply and effectively prevented by preoperative administration of a 10% glucose solution by gastric tube In view of these facts we assume that the period of preoperative fasting was the principal cause of the metabolic acidosis during the operation The basal metabolism of normal infants with a body weight of 3-10 kg is about 50 Cal/kg/24 hours (Karlberg 1952), which is very high in comparison with adults

The disadvantage of preoperative administration of a glucose solution by gastric tube is that it increases the risk of regurgitation with aspiration In their study of deaths associated with anaesthesia, Edwards et al (1956) described how pre operative administration of a glucose solution to diabetic patients led to fatal regurgitation According to Morton and Wylie (1951), regurgitation can be regarded as a passive process In the horizontal patient the gravitational force can cause fluid to flow from the stomach, particularly if the gastro-oesophageal junction has been rendered incompetent by the presence of a tube If one nevertheless wants to use

this method, a very careful dosage scheme is imperative Fluids still present in the stomach must be removed by applying suction to the gastric tube, and a smooth induction technique is required The safest way to prevent metabolic acidosis would seem to be to reduce the period of preoperative fasting to a minimum and to give the infants priority on the operation schedule

The $P_{\zeta O_2}$ of the atrial blood in our group of spontaneously breathing patients was very high if compared with the values reported by others in non-anaesthetized infants (Albert and Winters 1966, Blomer and Hahn 1963, Cook et al 1957) The value was also much higher than that in the hydrocephalics we examined before the operation. Values exceeding 60 mm Hg were found in some cases, although the same technique of anaesthesia was used in all patients of this group It would have been of importance to determine the acid-base state of the capillary blood at the same time as that of the atrial blood samples But this was impossible for technical reasons (the micro-Åstrup method had not yet been introduced in our clinic at that time) Since according to Rahn and Fenn (1955) the P_{CO_2} of central venous blood primarily depends on ventilation, the values we found are suggestive of hypoventilation in this group The values obtained immediately after the switch-over to IPPV revealed an immediate decrease in $P_{\zeta O_2}$ The hypoventilation of spontaneous respiration can be completely avoided by keeping infants under IPPV throughout the period of endotracheal anaesthesia (table IV)

The slight decrease in $P_{\zeta O_2}$ observed after starting IPPV was too small to suppress cardiac function to any marked extent The decrease observed was much smaller than the values found in various publications in relation to a change in cardiac output In protracted IPPV, $P_{\zeta O_2}$ values were attained at which an influence on cardiac output is likely according to the equation of Prys-Roberts et al (1967b)

We are currently using intravenous or intramuscular succinylcholine when applying IPPV. After succinylcholine relaxation the patient is intubated and connected to the SIV A single dose of succinylcholine is usually sufficient for adequate IPPV The anaesthetic gas mixture we use consists of oxygen, nitrous oxide and a volatilized anaesthetic Unlike Salanitre and Rackow (1961), we have had no unfavourable experience with succinylcholine in infants These authors maintained that a very careful watch must be kept against a decrease in temperature because the subject cannot shiver under these conditions

Our observation of a decrease in mean oxygen saturation of the atrial blood after changing to IPPV was in agreement with a report by Kuyper (1965), the phenomenon was also mentioned by Dobkin (1969) Table III shows that the standard deviation of the mean oxygen saturation of right atrial blood was very large The lowest value was 30% (patient 66/15896) In this case the high $P_{\zeta O_2}$ (64 mm Hg) indicated marked hypoventilation But in several other patients with oxygen saturations of less than 50% there was no question of marked hypoventilation, on the other hand the group includes patients with a high saturation and a distinctly increased $P_{\zeta O_2}$ (patients 68/382, 69/6868 and 69/6294) In our technique of

anaesthesia we made use of a high FI_{O_2}. Hypoventilation of certain lung parts due to obstruction was eliminated by painstakingly careful localization of the endotracheal tube. Our patients were free from cardiac and pulmonary abnormalities. No cyanosis was observed at the field of operation. In view of these facts, and because a high FI_{O_2} was used, we assume that arterial blood oxygenation in our patients was good as long as the P_{CO_2} was not markedly increased. The standard deviation of the saturation values was not smaller during IPPV than during spontaneous respiration. The large standard deviation must therefore have been due to the fact that blood samples obtained from the right atrium in infants are not representative of true mixed venous blood. Our patients have such small atria and the localization of the catheter was so random that much of the blood sample probably came from a particular flow, e.g. from the coronary sinus in many cases. This view is in agreement with that of Barrat-Boyes and Wood (1957), who maintained that true mixed blood can only be obtained from the pulmonary artery. Since our blood samples were obtained through catheters randomly localized in the atrium, we attributed to the decrease in saturation measured the same significance as to that in blood samples obtained from the pulmonary artery. Theye and Tuohy (1965) did likewise. According to Rahn and Fenn (1955), a decrease in the oxygen tension of central venous blood is based primarily on a decrease in cardiac output. This contention is supported by the fact that, in Kuyper's test animals, the oxygen consumption showed no significant change upon switch-over from spontaneous respiration to IPPV.

Our experimental set-up gave no information on the extent of the decrease in cardiac output. We calculated that the P_{O_2} of our samples decreased significantly after starting IPPV. This raises the question whether the decrease in cardiac output as a result of IPPV can give rise to insufficiency of the oxygen supply to the tissues.

Bendixen and Laver (1965) believed that it is impossible to indicate a common critical P_{O_2} value for all tissues (the critical P_{O_2} being the pressure below which oxygenation of respiratory enzymes is insufficient). They assumed that this value ranges from 20 to 30 mm Hg, with exceptions in both directions. According to Howell (1966), the relationship between venous P_{O_2} and intracellular P_{O_2} depends on: oxygen consumption, the spatial configuration of blood capillaries, and the characteristic features of the diffusion route from blood capillaries to intracellular enzymes. He believed that the venous P_{O_2} can be an index of tissue oxygenation at rest, but not during exercise. Mitchell et al. (1958) found that, during strenuous treadmill exercise, the Sa_{O_2} decreased while the P_{O_2} in the femoral venous blood hardly changed, although tissue hypoxia had to be present. Robinson (1967) established that, during anaesthesia with controlled hypotension, no EEG changes occurred until the P_{O_2} in the bulb of the jugular vein fell below 35 mm Hg. At a systolic blood pressure of 50 mm Hg, the P_{O_2} was still 50 mm Hg. When the blood pressure then decreased to 20 mm Hg, the P_{O_2} in blood from the bulb of the jugular vein diminished to 10 mm Hg. Robinson concluded from this finding that, at a

blood pressure of 50 mm Hg, the cerebrum is capable of extracting still more oxygen from the blood if perfusion diminishes further Assuming that no shunts existed, therefore, there could have been no cerebral hypoxia at a blood pressure of 50 mm Hg Our impression is that this conclusion does not apply when 'retractor anaemia' occurs in the course of intracranial interventions Lubbers (1966) believed that the question of the presence of tissue hypoxia cannot be answered by analysing mixed venous or arterial blood McDowall (1970) supported this in the statement that a sufficient $S\bar{v}_{O_2}$ is not conclusive of normal cerebral oxygenation The cerebral venous return amounts to 15% of the total venous return If the cerebral venous oxygen saturation decreases from 60% to 30%, then the $S\bar{v}_{O_2}$ diminishes by only 5% Brewish (1969) likewise believed that the problem of tissue hypoxia is still unsolved He maintained that the P_{O_2} of mixed venous blood gives too generalized an impression, whereas the local tissue P_{O_2} is of too limited significance The P_{O_2} of venous blood from an organ can vary widely The kidney is lavishly perfused but extracts little oxygen from the blood The perfusion of the myocardium is much smaller, but its oxygen consumption much higher

In the absence of unequivocal criteria to be used in establishing hypoxia of certain tissues, we assume with Bendixen and Laver (1965) that tissue oxygenation is sufficient as long as the P_{O_2} of central venous blood is between 20 and 30 mm Hg – unless there are reasons to think otherwise for some tissues Since the P_{O_2} of the blood samples from the right atrium averaged over 40 mm Hg in our patients, oxygenation must in our opinion have been sufficient

2 CHANGES IN OESOPHAGEAL PRESSURE

Table VI shows that the mean oesophageal pressure amplitude in our spontaneously breathing infants under endotracheal anaesthesia was smaller than the values reported by various investigators in non-anaesthetized infants (McIlroy and Tomlinson 1955, Cook et al 1957, Krieger 1963)

Since a low pressure amplitude during spontaneous respiration results in a low transpulmonary pressure, this also implies a small distension or tidal volume of the lungs The respiratory minute volume is likewise bound to be small, for the mean respiratory rate in our patients did not differ so much from the normal that the small tidal volume was compensated by a higher respiratory rate

The study of the end-expiratory oesophageal pressure in patients given IPPV after succinylcholine relaxation, revealed a significant increase of this pressure This increase persisted after discontinuation of IPPV We have explained the increase by assuming that the volume of the thorax diminished and that, as a result, the pressure in chest compartments not communicating with the atmosphere increased According to Comroe et al (1957), the resting position of the lungs outside the thorax is smaller than the residual volume But the resting position of the thorax without lungs is at a much greater volume than when the respiratory system is intact In adults, the volume of the thorax alone amounts to 70% of the

vital capacity In infants, this outward recoil of the chest wall hardly occurs (Agostoni 1970) Succinylcholine relaxation causes a disturbance of the equilibrium in the respiratory system The activity of the respiratory muscles, particularly those of the diaphragm, is abolished The elastic strength of the lungs and the forces of surface tension in the lungs, and possibly also the upward pressure exerted by the abdominal contents, then cause partial collapse of the thorax This collapse does not increase when IPPV is discontinued and the gas flow turned off This means that there was no pre-existent increase in functional residual capacity as a result of resistance to the gas flow in the narrow endotracheal tube which the respiratory musculature could not overcome For, blocking of the potential energy in the respiratory musculature immediately causes partial collapse of the thorax and the lung volume This is confirmed by the fact that, after discontinuation of IPPV, the transpulmonary pressure is found to have diminished as compared with the transpulmonary pressure during spontaneous respiration Moreover, at a second succinylcholine relaxation after resumption of spontaneous respiration, the end-expiratory oesophageal pressure shows no further significant change from the value found after resumption of spontaneous respiration but before the second relaxation The fact that, after resumption of spontaneous respiration following the first dose of succinylcholine, the end-expiratory oesophageal pressure remains higher than the initial value, is indicative of a secondary effect due to muscle relaxation The subatmospheric intrathoracic pressure is the result of the equilibrium between the tonus of chest wall and diaphragm, and the retractile strength of the lungs The former forces are eliminated by succinylcholine, and consequently the intrathoracic pressure becomes less negative, as manifested by the elevation of the end-expiratory oesophageal pressure The transpulmonary pressure diminishes, and the functional residual capacity decreases as a result After exhaustion of the effect of the first dose of succinylcholine, spontaneous respiration is gradually resumed but apparently the pre-existent equilibrium is not quickly restored This is why a number of deep sighs are not visible on the oesophagograms Perhaps restoration of the original equilibrium is further impeded by the fact that lung compliance is reduced by the anaesthesia (McClenahan 1966, Reynolds and Etsten 1966, Lunn 1968b, Patterson and Sullivan 1968, Forrest 1970) and the outward recoil of the chest wall is inconsiderable (Agostoni 1970)

In view of the above described findings we agree with Ayre (1937) and Wawersik (1967) that the increase in respiratory resistance caused by the endotracheal tube constitutes no insurmountable obstacles to the respiratory musculature The fact that the increased demands in terms of respiratory work (Reynolds and Etsten 1966, Wawersik 1967) cannot be met (as manifested by hypoventilation) may have the following possible causes

a Depression of respiration caused by the anaesthetics (N_2O and penthrane) This is the principal cause of the hypoventilation Accordingly, controlled ventilation is very easy in these patients

b Sensitization of vagal stretch and deflation endings in the lungs produces a superficial type of respiration with an increased respiratory rate on a more inspiratory level (Whitteridge 1958)

c The resistance due to the endotracheal tube reflexively increases the functional residual capacity In spontaneous respiration of the type shown by our patients, this factor is of no significance On the basis of data supplied by Harrison (1964) and Lunn (1968a), we estimate the inspiratory peak flow to be at most 2 l/min, the corresponding resistance is only 0 5 cm H_2O/l/min

In view of our findings it is meaningless to support expiration by applying negative pressure during controlled ventilation After succinylcholine muscle relaxation, the end-expiratory oesophageal pressure level is not lowered upon temporary discontinuation of IPPV But there is no question of any active effort on the part of the patient in expiration, and during IPPV the tidal volume exceeds that during spontaneous respiration (because of the decreased P_{CO_2} with a lower respiratory rate)

As the mean ventilation pressure is conducted to the oesophageal pressure, a pressure loss of some 80% occurs as a result of the small lung compliance the mean ventilation pressure is 6 cm H_2O and the mean oesophageal pressure in relation to the end-expiratory pressure is +1 1 ± 0 5 cm H_2O

During IPPV, transpulmonary pressure and lung distension are increased, taking into account the insufficient spontaneous respiration This may have its consequences for the resistance of the pulmonary vascular bed In our experimental set-up a detailed analysis of this resistance was impossible According to Roos et al (1961) and Donald (1962), major changes in the resistance of the pulmonary vascular bed after starting IPPV are unlikely because the change in transpulmonary pressure is only small (+2 8 cm H_2O) The extent to which absence of changes in resistance also prevails in infants cannot be established with certainty

3 CHANGES IN RIGHT ATRIAL BLOOD PRESSURE

We found no significant changes in mean effective right atrial filling pressure in response to IPPV This finding disagrees with reports in the literature (Cournand et al 1948, Werko 1947, Aoyagi and Piiper 1965) The large standard deviation (± 2 4 cm H_2O) is a conspicuous feature Since the individual spontaneous variation in atrial pressure is only 0 5 cm H_2O during spontaneous respiration and 0 7 cm H_2O during IPPV, the large standard deviation cannot be due to the variability of central venous pressure mentioned by Green (1948), nor to inaccuracies in determinations of pressure According to Werko (1947), the relatively wide variation of the effect of controlled ventilation on the circulation in different patients is explained by the fact that the conduction of the pressure to the various intrathoracic organs is so variable In view of the close topographic interrelationship of the mediastinal organs, we believe that conduction of the ventilation pressure to the right atrium is not more variable than that to the oesophagus During spontaneous respiration as

well as during IPPV, variations in respiratory pressure are always found to be conducted clearly and simultaneously to oesophagus and right atrium

Assuming on the authority of Sarnoff (1955) that the effective right atrial filling pressure is a yardstick of the stroke work supplied by the right ventricle, the unpredictable behaviour of this pressure might be ascribed to the fact that different influences of the type of respiration on the pulmonary vascular resistance occur in these infants In the entire group, the increased lung distension had no significant consequences for the effective right atrial filling pressure (and thus for the right ventricular stroke work) This factor, therefore, cannot have contributed to the decrease in cardiac output observed

Another factor in determining the effective right atrial filling pressure is the venous return The increase in intrathoracic pressure caused by IPPV causes reduction of the venous return and therefore a decrease in cardiac output We have no detailed information on the degree of reduction of the venous return This, too, may show marked individual variations The large standard deviation of the individual decrease in oxygen saturation might indicate this The behaviour of the effective right atrial filling pressure after starting IPPV might then be determined in individual cases by the combined influence of the change in venous return to the right heart and possible small changes in pulmonary vascular resistance According to Sarnoff (1955), an increase of the resistance in the systemic circulation has no immediate consequences for right ventricular stroke work

During long-term endotracheal anaesthesia, spontaneous respiration in infants is insufficient This is indicated by the high carbon dioxide pressure in right atrial blood and by an oesophageal pressure amplitude which is low if compared with data from the literature The small respiratory excursions are not adequately compensated by an increase in respiratory rate The resistance of the endotracheal tube is not an important factor in the aetiology of the respiratory insufficiency This was demonstrated by determination of the end-expiratory oesophageal pressure before and after succinylcholine relaxation According to the literature it is possible that the resistance of the endotracheal tube reflexively leads to a type of respiration with increased functional residual capacity In our patients this factor would seem to be of small importance because respiration was so depressed that a low inspiratory peak flow encountered only slight resistance in the endotracheal tube (with the 16 French tubes commonly used, less than 0 5 cm H_2O/l/min)

A type of respiration with increased functional residual capacity can also be caused by the influence of anaesthetics on the vagal stretch and deflation endings In combination with a small tidal volume, this contributes to insufficiency of the gas exchange We consider the depressant effect of gaseous and volatilized anaesthetics on the respiration to be the principal cause of the respiratory insuf ficiency This conclusion is based on the low oesophageal pressure amplitude during spontaneous respiration and the ease with which controlled ventilation can be carried out in these cases, this indicates inconsiderable activity of the respiratory musculature

IPPV prevents respiratory insufficiency during anaesthesia It is unnecessary to support the passive expiratory phase by applying subatmospheric pressure in infants The duration of inspiratory and expiratory phase should be sufficient to ensure adequate gas transport through the endotracheal tube An inspiratory phase of 1 sec is sufficient Mechanically controlled ventilation is quite superior to manually controlled ventilation The ventilator used in our study produces a ventilation curve which corresponds to Cournand type III During spontaneous respiration, no increase of pressure occurs before the endotracheal tube in our anaesthetic system In agreement with theoretical considerations we found that, even with depressed respiration, the mean oesophageal pressure amplitude during IPPV was lower than that during spontaneous respiration

IPPV leads to an increase in mean intrathoracic pressure Succinylcholine relaxation also causes this increase The pressure remains increased after resumption of spontaneous respiration, this suggests that the equilibrium which previously existed between lungs and chest wall in the respiratory system, is not immediately restored Due to the small lung compliance in infants, only some 20% of the mean ventilation pressure is conducted to the oesophagus

IPPV causes a decrease in cardiac output The principal cause of this decrease is the diminution of venous return The change in pulmonary vascular resistance due to increased lung distension is not so marked as to exert a significant influence on right ventricular stroke work

In infants, blood samples obtained from the right atrium are not representative of mixed venous blood Complete admixture occurs only past the right atrium The decrease in central venous oxygen saturation calls for the use of a high FI_{O_2} during anaesthesia with IPPV However, a FI_{O_2} of 50% is unnecessary because at a FI_{O_2} of 40% the tissues are capable of extracting more oxygen from the blood if tissue perfusion diminishes

Protracted fasting readily leads to metabolic acidosis This can be avoided by preoperative administration of a 10% glucose solution by gastric tube According to the literature, however, this procedure gives an increased mortality due to regurgitation It is therefore safer to avoid the metabolic acidosis as much as possible by giving infants priority on the operation schedule

The sufficiency of respiration in spontaneously breathing infants during endotracheal anaesthesia is a controversial subject Many authors maintain that the respiratory resistance due to the narrow endotracheal tube is an important factor in the aetiology of respiratory insufficiency Others disagree In this study we have tried to settle this question We have also studied the influence of intermittent positive pressure ventilation (IPPV) on ventilation and circulation The patients we examined were infants treated for progressive hydrocephalus by a ventriculo-atrial shunt procedure This intervention entails no mechanical disturbance of the respiratory mechanism The sacrifice of an internal jugular vein exerts no influence on the drainage of blood from the craniocervical region (chapter I)

According to the literature, the $Pa_{(O_2}$ in infants is lower than that in adults The same applies to the base excess, but not to the actual pH The static and dynamic lung compliances in infants are small But the compliance of the chest wall is so large that the total compliance is determined mainly by the lung compliance The resistance in the respiratory tract in infants is 10 15 times as high as that in adults As in adults, the respiratory work in infants is dependent on the respiratory rate The respiratory work per square metre of body surface is about the same in infants as in adults During endotracheal anaesthesia, respiratory resistance and respiratory work show a marked increase, while the lung compliance diminishes Factors of importance in this respect include the $PA_{(O_2}$ and $Pa_{(O_2}$ Anaesthetic agents and endotracheal tube can reflexively cause an increased functional residual capacity The respiration in a group of patients with internal hydrocephalus proved not to differ significantly from that in normal infants During anaesthesia – whether with spontaneous respiration or with IPPV – pulmonary venous admixture increases and a decrease in cardiac output occurs As a result, the effect of the venous admixture increases Dependent on the percentage of venous admixture, hyperventilation can thus cause a paradoxical fall of the Pa_{O_2} (chapter II)

In our patients, we examined the following parameters during spontaneous respiration and during IPPV a oxygen saturation and acid-base state in blood samples from the right atrium, b oesophageal pressure amplitude, the change in mean oesophageal pressure and the behaviour of the end-expiratory oesophageal pressure after succinylcholine relaxation, c the behaviour of the blood pressure in the right atrium and the effective right atrial filling pressure IPPV was carried out with the aid of the Sheffield Infant Ventilator (SIV), which produces a ventilation pressure curve commonly known as Cournand type III (chapter III)

According to some investigators, blood from the right atrium can be regarded as representative of mixed venous blood Changes in the oxygen saturation of this blood indicate a change in cardiac output Changes in the carbon dioxide pressure are

primarily dependent on ventilation The metabolic components of the acid-base state correspond with those of arterial blood

Many authors maintain that changes in oesophageal pressure due to respiration or controlled ventilation are a good parameter for the changes in intrathoracic pressure and in pressure around the right atrium The oesophageal balloon is preferably positioned in the middle one-third of the oesophagus

The effective right atrial filling pressure is a yardstick of the right ventricular stroke work The pressure is calculated from the value of the mean atrial blood pressure minus that of the mean oesophageal pressure Most investigators report an increase of effective right atrial filling pressure upon starting controlled ventilation (chapter IV)

Our study has shown that spontaneous respiration in infants during protracted endotracheal anaesthesia is insufficient This is ascribed to the depressant effect of the gaseous and volatilized anaesthetics used, but not to the increase in respiratory resistance due to the endotracheal tube IPPV prevents respiratory insufficiency during anaesthesia The duration of the inspiratory and the expiratory phase should be sufficient to ensure an adequate gas transport through the narrow endotracheal tube The use of a ventilator is to be preferred to manual control of ventilation

The use of subatmospheric pressure to support the expiratory phase is unnecessary IPPV leads to an increase in mean oesophageal pressure Succinylcholine relaxation also causes an increase As an after-effect of succinylcholine, the pressure remains increased for some time after resumption of spontaneous respiration the pre-existent equilibrium between lungs and chest wall in the respiratory system is not immediately restored

Although the cardiac output was not measured directly, we have concluded from indirect data that it decreases The decrease is chiefly based on diminution of the venous return to the heart as a result of the increased intrathoracic pressure caused by IPPV The effective right atrial filling pressure is not significantly changed The same applies to the pulmonary vascular resistance, although this shows unmistakable individual variations According to theoretical considerations, it should make an essential difference for the pulmonary vascular resistance whether a given transpulmonary pressure is achieved by spontaneous respiration or by IPPV

The oxygen saturation of right atrial blood in infants, unlike that in adults, is not representative of that of true mixed venous blood from the pulmonary artery

Preoperative fasting readily leads to a state of metabolic acidosis in infants Administration of a 10% glucose solution by gastric tube from 3 hours after the last feeding until induction of anaesthesia can prevent this acidosis In view of possible regurgitation and aspiration, however, a very careful dosage scheme and a smooth induction technique are imperative The safest method to avoid metabolic acidosis is to give infants priority on the operation schedule (chapters V and VI)

Samenvatting

Er bestaan verschillende inzichten betreffende de sufficientie van de ademhaling van spontaan ademende zuigelingen in endotracheale narcose Vele auteurs menen dat de ademweerstand vanwege de nauwe endotracheale buis een belangrijke factor is voor het ontstaan van ademinsufficientie Anderen zijn deze mening niet toegedaan In dit onderzoek hebben wij getracht op deze vraag een antwoord te geven Wij gingen eveneens de invloed na van intermitterende positieve drukbeademing (IPPV) op de ventilatie en de circulatie De door ons onderzochte proefpersonen waren zuigelingen bij wie wegens behandeling van progressieve hydrocefalus een ventriculo-atriale shunt werd aangelegd Deze ingreep geeft geen mechanische verstoring van het ademhalingsmechanisme Het opofferen van een v jugularis interna heeft geen invloed op de afvloed van bloed uit het hoofd-halsgebied (hoofdstuk I)

Volgens de literatuur is de Pa_{CO_2} bij zuigelingen lager dan bij volwassenen Behalve voor de Pa_{CO_2} geldt dit ook voor het base overschot, doch niet voor de actuele pH De statische en dynamische compliance van de longen van zuigelingen zijn klein De compliance van de thoraxwand is echter zo groot dat de totale compliance in hoofdzaak wordt bepaald door de longcompliance De luchtwegweerstand is 10 tot 15 × zo groot als bij volwassenen Evenals bij deze is de ademarbeid afhankelijk van de ademfrequentie Per m^2 lichaamsoppervlak is de ademarbeid van zuigelingen ongeveer even groot als van volwassenen In endotracheale narcose nemen de luchtwegweerstand en de ademarbeid sterk toe De longcompliance neemt af De PA_{CO_2} en Pa_{CO_2} zijn hierop o m van invloed Narcotica en endotracheale buis kunnen reflectoir een verhoogd functioneel residu veroorzaken De ademhaling van een groep patienten met hydrocefalus internus blijkt niet significant te verschillen met die van normale zuigelingen Tijdens de narcose, met spontane ademhaling of beademing, neemt de pulmonale veneuze bijmenging toe en treedt een daling van het hart-minuutvolume op Hierdoor wordt het effect van de pulmonale veneuze bijmenging groter Afhankelijk van het percentage veneuze bijmenging kan door hyperventilatie zodoende een paradoxale daling van de Pa_{O_2} optreden (hoofdstuk II)

Bij onze patienten onderzochten wij voór en na het overgaan op IPPV de volgende parameters a bloedmonsters uit het rechter atrium op O_2 verzadiging en zuur-base status, b de amplitudo van de oesofagusdruk, de verandering in de gemiddelde oesofagusdruk, en het gedrag van de eindexpiratoire oesofagusdruk na relaxeren van de patienten met succinylcholine, c het gedrag van de bloeddruk in het rechter atrium en de effectieve vuldruk van het rechter atrium IPPV werd verricht met een beademingsapparaat de Sheffield Infant Ventilator Deze bewerkstelligt een beademingsdrukcurve volgens Cournand type III (hoofdstuk III)

Volgens sommige onderzoekers mag men bloed uit het rechter atrium representatief achten voor gemengd veneus bloed. Veranderingen in de O_2-verzadiging hiervan duiden op een verandering van het hart-minuut-volume. Veranderingen in de CO_2-spanning zijn in de eerste plaats afhankelijk van de ventilatie De metabole componenten van de zuur-base status komen overeen met die van het arteriele bloed.

Veranderingen van de oesofagusdruk door ademhaling of beademing zijn volgens vele auteurs een goede parameter voor de veranderingen in de intrathoracale druk en de druk om het rechter atrium. De oesofagusballon wordt bij voorkeur in het middelste derde gedeelte van de oesofagus geplaatst

De effectieve vuldruk van het rechter atrium is een maatstaf voor de slagarbeid van de rechter ventrikel De druk wordt berekend uit de waarde van de gemiddelde atriale bloeddruk minus de gemiddelde oesofagusdruk De meeste onderzoekers vinden bij beademen een stijging van de effectieve vuldruk van het rechter atrium (hoofdstuk IV).

Uit ons onderzoek blijkt dat de spontane ademhaling tijdens een langdurige endotracheale narcose bij zuigelingen insufficient is. Dit wordt toegeschreven aan het deprimerende effect op de ademhaling van de toegepaste gas- en dampvormige narcotica, doch niet aan de verhoging van de ademweerstand door de endotracheale buis. IPPV voorkomt ademinsufficientie tijdens de narcose De duur van de in- en expiratiefase moet voldoende zijn om een adequaat gastransport door de nauwe endotracheale buis naar en van de alveoli mogelijk te maken Het gebruik van een ventilator is te verkiezen boven manuele beademing.

Het gebruik van een subatmosferische druk ter ondersteuning van de uitademing blijkt niet nodig te zijn. IPPV geeft een stijging van de gemiddelde oesofagusdruk. Deze stijgt eveneens door relaxeren met succinylcholine Als na-effect van de werking van succinylcholine blijft de druk enige tijd verhoogd nadat de spontane ademhaling weer is teruggekeerd het tevoren in de tractus respiratorius bestaande evenwicht tussen longen en thoraxwand herstelt zich niet direct

Alhoewel het hart-minuut-volume niet direct werd gemeten, wordt uit indirecte gegevens geconcludeerd dat dit afneemt De daling berust hoofdzakelijk op een vermindering van de veneuze afvloed naar het hart doordat IPPV de intrathoracale druk verhoogt. De effectieve vuldruk van het rechter atrium verandert niet significant. Hetzelfde geldt voor de longvaatweerstand, alhoewel hier duidelijke individuele schommelingen aanwezig zijn Op grond van theoretische overwegingen moet het voor de weerstand in het pulmonale vaatbed principieel verschil uitmaken of een bepaalde transpulmonale druk wordt verkregen door de eigen ademhaling of door IPPV.

In tegenstelling tot bevindingen bij volwassenen is de O_2-verzadiging van het bloed uit het rechter atrium van zuigelingen niet representatief voor die van gemengd veneus bloed uit de a. pulmonalis

Zuigelingen geraken door prae-operatieve voedselonthouding gemakkelijk in een

toestand van metabole acidose. Het toedienen van sol.glucose 10% per maagsonde vanaf 3 uur na de laatste voeding tot de inleiding van de narcose kan deze acidose voorkomen. Vanwege de mogelijkheid van regurgitatie en aspiratie is echter een zorgvuldig doseringsschema noodzakelijk, alsmede een vlot verlopende inleiding van de narcose. De veiligste methode ter voorkoming van de metabole acidose is het verlenen van prioriteit aan zuigelingen in het operatieprogramma (hoofdstuk V en VI).

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J thorac. cardiovasc. Surg., **52**, 105.

STELLINGEN

I. De ademinsufficientie van zuigelingen onder endotracheale narcose wordt niet veroorzaakt door de ademweerstand als gevolg van de nauwe endotracheale tube.

II Het toepassen van met ethyleen-oxide gesteriliseerde endotracheale tubes is gecontraindiceerd voor lijders aan rheumatoide arthritis
Krisher, J A (1969). *Surg Clin. N Amer.*, 49,757.

III. Het is ongewenst om in de praeoperatieve voorbereiding van hypertensie patienten de medicatie met antihypertensiva te onderbreken
Prys Roberts, C et al. (1971) *Brit. J Anaesth.*, 43,122.

IV. Het routinematig voorschrijven van atropine in de praemedicatie betekent voor de patient een overbodige belasting

V. Gedurende de narcose met kunstmatige verlaging van de bloeddruk, is het gebruik van lachgas gecontraindiceerd.
Ty Smith, N. et al. (1970) *Anesthesiology*, 32, 410

VI. De toepassing van hypercarbie bij de narcose voor endarterectomie van de a carotis is niet de oplossing voor het vraagstuk van een zo adaequaat mogelijke cerebrale perfusie tijdens deze ingreep.
Ehrenfeld, W. K. et al. (1970) *Surgery*, 67,87.

VII. Massa onderzoek ter vroegtijdige opsporing van borstkanker kan het beste door middel van de thermografie geschieden
Aarts, N. J M. (1968) *Proceedings of the first international symposium on detection of cancer* Spa, 341–347

VIII. Het is noodzakelijk om bij het radiologisch onderzoek van hypofyse tumoren naast een ventriculo-cysternografie een dubbelzijdige carotis arteriografie te verrichten.

IX. De levensduur van neonaten met een meningo-myelocèle, uitgebreide verlammingsverschijnselen en een hoofdomtrek welke de 90-percentiel met 2 cm overschrijdt, wordt door intensieve behandeling niet verlengd.
Lorber, J. (1971): *Develop. Med. Child Neurol.*, 13,279.

X. Het verdient aanbeveling om de intraveneuze dosering van medicamenten met een geringe therapeutische breedte, aan te geven in mg/kg/tijdseenheid.

XI. Het is overbodig om in medische publicaties de getallenreeksen te vermelden welke dienden tot het berekenen van de relevante gemiddelde waarden met de standaard afwijkingen.

XII In de opleiding tot arts dient een co-assistentschap in de anesthesiologie te worden opgenomen.

XIII. Sinds de vara-haan ophield te kraaien is hij roder geworden.

H. J. Teijen. Nijmegen, 9 december 1971.